IN THE UNITED STATES DISTRICT COURT
FOR THE NORTHERN DISTRICT OF TEXAS
DALLAS DIVISION

UNITED STATES OF AMERICA	)	3:15-CR-496-L
	)	
v.	)	Daubert Hearing
	)	
USPLABS, et. al.	)	May 9, 2018

BEFORE THE HONORABLE RENEE HARRIS TOLIVER
United States Magistrate Judge
In Dallas, Texas

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(May 9, 2018.)

THE COURT: This is case number 3:15-CR-496-L. May I have announcements, please. For the record.

MS. MARTIN: Yes, Your Honor. Errin Martin for the Government and I have with me Patrick Runkle and David Sullivan from the Consumer Protection Branch of the Department of Justice.

MR. WEINGARTEN: Good morning, Your Honor. Reid Weingarten for the Defendant USPLabs. With me is Chris Niewoehner, Patrick Linehan, and David Fragale.

MR. GIBSON: Good morning, Your Honor. Michael Gibson here for the Defendant Jacobo Geissler. We are present and ready to go. He is here in the back.

THE COURT: Thank you.

MR. WEILAND: Good morning, Your Honor. I'm Steven Cass Weiland for the Defendant Matt Herbert. With me today is my partner, Bobby Hawkins.

MR. WEBSTER: Your Honor, may it please the Court. Bob Webster for Defendant No. 8, Cyril Willson who is also present.

THE DEFENDANT: Your Honor, Joe Shearin on behalf of Kenneth Miles.

MR. ROPER: Richard Roper on behalf of Jonathan Doyle with me is -- Thompson & Knight law firm.

MR. HALL: Patrick Hall on behalf of Defendant Patel

who is sitting next to me here.

MR. MCMULLEN: Good morning, Your Honor. Joseph McMullen, here for SK Labs.

THE COURT: My plan is this: First of all, we have blocked out today and tomorrow, if needed to conclude the hearing on these matters. Unless you tell me otherwise, I will consider an argument or evidence presented by a codefendant to apply equally to all the defendants so that you don't feel like you have to have anything. My plan today so to take those motions that the parties intend to present live witnesses for first, just for the convenience of the witnesses. And then to proceed to those that require only argument after that.

As far as the secondary order, it will be by motion and what I will ask you to do is to -- because we have so many motions we are considering today, when you're presenting testimony to remind me which motions or motion it relates to at the start. I'm assuming because we are dealing with experts nobody is invoking the rule. Am I wrong about that? If there are witnesses in the courtroom we can go ahead and swear in?

MS. MARTIN: Yes, Your Honor.

THE COURT: If those witnesses could approach the bar, please. Gentlemen, will reach of you state your name.

THE WITNESS: My name is Karl Klontz. I'm a

physician.

THE WITNESS: Herbert Bonkovsky. Physician.

THE COURT: Dr. Klontz, Dr. -- I'm going to butcher your name until I've heard it again several times.

THE WITNESS: Bonkovsky.

THE COURT: Bonkovsky. Will you please raise your right hand and be sworn.

(Two witnesses sworn.)

THE COURT: Thank you. And with that said, I'll need to know, are we going to proceed then on the motions to exclude the two doctors first? Is that --

MR. RUNKLE: I believe that's right, Your Honor.

THE COURT: All right. Then I'm ready.

MR. SULLIVAN: May it please the Court. David Sullivan on behalf of the United States. I call Dr. Herbert Bonkovsky to the stand.

HERBERT BONKOVSKY, GOVERNMENT WITNESS, was sworn

DIRECT EXAMINATION

BY MR. SULLIVAN:

Q. Good morning, Dr. Bonkovsky.

A. Good morning.

Q. Could you please state your name for the record?

A. Herbert L. Bonkovsky.

Q. And what is your occupation?

A. I am a physician and investigator.

Q. And where do you currently work?
A. My primary work is at Wake Forest University School of Medicine and the North Carolina Baptist Hospital in Winston Salem, North Carolina.
Q. What's your current position, your present title?
A. I'm a Professor of Medicine and also molecular medicine and translational science there and the Director of Liver Services, the litter service line for the hospital system. I also am the Director of the Laboratory For Liver and Metabolic Disorders Research.
Q. Are you also a professor of medicine at University of North Carolina Chapel Hill?
A. Yes.
Q. And you also are the adjunct professor of biology at the University of North Carolina at Charlotte?
A. Yes.
Q. Are you also a Professor of Medicine at the University of Connecticut Health Center in Farmington, Connecticut?
A. Yes.
Q. When did you obtain your undergraduate degree and where from?
A. I graduated in 1963 from Early College, Richmond, Indiana.
Q. What was your degree in?
A. Major in chemistry and minor in philosophy.
Q. And you were the valedictorian of your class?

A. Yes.
Q. And where did you receive your M.D.?
A. From Case Western Reserve University School of Medicine in Cleveland, Ohio, in 1967.
Q. When I look at your CV, you have a lot of acronyms behind your name. Could you tell the Court what those acronyms state?
A. I think the first one on the list is FAASLD. That stands for Fellow of the American Association For the Study of Liver Diseases; I am a member and fellow as well of the American College of Gastroenterology, so FACG; a fellow of the American College of Physicians, FACP; and a fellow of the American Gastroenterology Association. That's usually abbreviated AGAF. And, let's see. I think there's one more. Maybe not. I can't remember now. Did I get them all?
Q. I think so. When did you first become licensed as a physician?
A. In 1968.
Q. And in reviewing your CV, sir, I see that you held medical licenses in several states. Where are you currently licensed?
A. In North Carolina.
Q. And did you ever receive a specialty in medicine?
A. Yes. I first became a specialist in the general field of internal medicine in 1973 and followed that with subspecialty certification in gastroenterology in 1967.

Q. And in reviewing your CV I see that you've held around 35 positions of employment throughout your career. Could you identify for the Court the positions that you held a position of leadership.

A. My first position of leadership was to establish and direct a GI liver unit at the VA affiliate of Dartmouth medical school in White River Junction Vermont and I rose through the ranks there from assistant to associate to full professor and then in 1985 accepted the position of professor of medicine and director of the General Clinical Research Center and the Clinical Research Unit at Emory University. I moved from Emory in 1990 to become the director of the GI and hepatology and nutrition position at the University of Massachusetts Medical Center in Worcester, Mass. and stayed there for about 12 years until moving for five years to the University of Connecticut Health Sciences Center in Farmington, Connecticut, where again I was director of the General Clinical Research Center and the Clinical Research Unit and then was recruited to be the vice-president for research for what was then called Carolina's health care system in Charlotte, mainly, basically in Charlotte, but facilities throughout the Carolinas. The name of that recently was changed to Atrium Health, so that's the current name, and then in January of 2015 moved my research programs to Wake Forest to continue with those activities.

Q. These positions you've held during your career, are they involved with you actively treating patients suffering from both liver and gastroenterological disorders?
A. Yes. Throughout my career I've been actively engaged as a practicing physician. I mainly do three things, the traditional three this of academic medicine: So patient care; education of medical students, residents, fellows, junior faculty; and research and the research has been both laboratory based and clinical research, so clinical investigation.
Q. And you are a hepatologist?
A. Yes.
Q. Would you explain to Judge Toliver what hepatology is, what a hepatologist does?
A. It's a subspecialty within the field of gastroenterology in which we concentrate on really liver and the biliary tract disorders in health and disease.
Q. You have been licensed now for 50 years? Almost 50 years?
A. Yes. Correct.
Q. And you've been board certified as specialist in internal medicine and gastroenterology since 1977?
A. Yes. Correct.
Q. All right. I notice by reviewing your CV that you've published or been a co-author of 442 peer review full papers?
A. That's correct.

Q. And you've also participated in 45 books or chapters of books regarding liver disorders?
A. Yes. Mainly liver. There have been some other things, but most of the books have been about liver disease. There are some others that are on metabolic disorders that affect the liver as one of the major organs.
Q. And you are currently the author of the chapter on Drug Induced Liver Injury and Saculin Boyer book on liver disease and hepatology?
A. Yes.
Q. That's one of the three or four primary texts for doctors to have learn about liver injuries?
A. Yes. It's one of the standard textbooks in the world on hepatology, the liver and its diseases.
Q. I also see you've been the author or co-author during your career of 370 abstracts?
A. Yes.
Q. And 50 brief reports or letters?
A. Yes.
Q. Dr. Bonkovsky, since you've been a specialist since 1977 and you actively treat patients with liver disorder, how many patients do you think you've treated in your career?
A. Must be at least 10,000. I, obviously, don't have really a count, but I continue to see patients every week at clinic sessions and rounds in hospital consultations and the like.

Q. So you are not just a doctor that read books and talks about stuff and lectures to students in classes; right?
A. No. I do, like I said, clinical practice as well as teaching and research.
Q. And you still get to teach. Is correct?
A. Yes.
Q. As a hepatologist, have you had the opportunity during your career to examine, diagnose, and treat patients that suffer from liver disorders?
A. Yes.
Q. Could you tell the Court what you do to treat these patients? If someone were to come to your clinic like from a referral from a doctor, from their primary care physician, and said my doctor thinks I have a liver disorder, what would you do upon presentation?
A. Well, the first thing is to take a thorough history and do a careful physical examination. Often times it will now be prior records that will be brought by the patient, sometimes sent ahead and scanned into electronic records, so I review those. Typically, in order to establish the most likely diagnosis, that initial evaluation will be followed by obtaining certain laboratory studies, particularly blood tests of various kinds, sometimes urine, sometimes other things and often, although not always, also include imaging of the liver, the liver tract or ultrasound or CT scan or MRI scan. Now a

days for many liver disorders, probably most MRI provides superior resolution and is most useful for differential diagnosis and at the end of that then we may recommend, depending on what is found in these studies, endoscopy, perhaps endoscopic ultrasound, perhaps ERCP, endoscopic retrograde cholangiopancreatography, perhaps liver biopsy. Sometimes there will be indication for doing exploratory surgery with direct observation of the liver and targeted biopsy, so it really depends upon the clinical situation.

Q. And different substances affect the liver in different ways. Is that correct?

A. Yes.

Q. So maybe acetaminophen would be different than something else or alcohol or something else. Is that correct?

A. Yes.

Q. And are there markers, in your experience from your review, that you could tell by looking at medical records, given your experience, what those different markers mean?

A. Well, there are typical presentations. So you mentioned alcohol. Excess alcohol is well known in some people, not all, can lead to both acute and chronic liver disease. It continues to be a major reason for the development of cirrhosis and cirrhosis just implies that there's been severe scar tissue that is formed in the liver due to a proinflammatory profibergenic stimulus, in this case let's say

it's alcohol. And the patterns of alcoholic hepatitis are that Marcus called the aminotransferases are moderately increased. They're not increased to a huge degree. It's rare for serum ALT AST to be greater than 500. For the bilirubin to be relatively high, the alkaline phosphates, which is another serum enzyme very useful in differential diagnosis to be elevated to also a modest degree, maybe up to 3 or 400. In contrast, you mentioned acetaminophen, the best known of the drugs and chemicals that are capable of causing acute liver injury which can be failure. The pattern is actually quite different. It is mainly a disease of overdose, user intended, suicidal intent, or sometimes unintended, just people take too many acetaminophen. It is in many different combinations of drugs, so they are not always aware they are getting an overdose and the acute hepatitis of acetaminophen hepatotoxicity is really quite different with the aminotransferase levels being in the thousands and the bilirubin not generally being all that elevated. Often times there will also be evidence renal insufficiently, sometimes pancreatitis as well, so there's a fairly typical signature, although there are other things besides acetaminophen that could produce something similar. And then -- So those are examples of intrinsic kinds of toxins by which we mean you or I or really anybody in this room who takes 100 extra strength Tylenol is likely to develop acute liver injury and perhaps

acute liver failure. More commonly, drugs that we know that are capable of causing liver injury, examples -- there are many examples, but common ones would be Augmentin, I.N.H., a variety of antibiotics, certain insects, particularly diclofenac. These things do not cause a predictable injury. They only cause injury in a relatively small minority of patients that take them, maybe one in hundred, one in thousand, sometimes one in a million. For example, probably many of us are taking statins for control of cholesterol, a very safe drug on the whole, but we know a few patients deliver serious liver injury from a statin. So that's an example of what appears to be immune mediated reaction that only causes injury in a small number of subjects and it probably has to do with post factors of certain genetic factors that influence the immune response to drugs and drug metabolism.

Q. So as a lawyer and a non-medical person -- All right. Is what you just said, simply put, that you can look at medical records and people's tests and you can say that this person obviously is suffering from an injury based upon alcohol or this or the other, there are markers that tell you certain things based on your experience and your work as a hepatologist?

A. Yes. One has to -- I guess you have to look fairly carefully at every case and come up with -- given the history,

the physical, all these other things that we've talked about, the most likely cause of liver injury in this case is excess alcohol, in the next case it might be excess acetaminophen, Augmentin, I.N.H.

Q. So if another physician would just bring you some medical records and said, "Hey, can you tell me if my patient is suffering from a liver disorder," would you as a hepatologist be able to look at those records, and if they were complete enough for you, to be able to make a determination if that person was suffering from a liver disorder?

A. Yes.

Q. Would any hepatologist with experience in the practice and the same type of credentials as you, would they be able to do the same thing?

A. Yes.

Q. Now, the criteria you mentioned earlier about reviewing medical records and blood work and MRIs and other types of testing, are those criteria and steps that you identified generally used by hepatologist in determining whether a person suffered from a liver injury?

A. Yes.

Q. In regards with this case, you've reviewed lots of different information regarding the toxic outbreak of 2013. Is that correct?

A. Yes.

Q. There were some papers you've read written by other folks, other doctors and whatnot, medical records you've looked at, and then the animal study conducted by scientists at the University of Arkansas. Is that correct?
A. Yes.
Q. When you reviewed those records and you look at the papers and you look at the study, is there a product that you identified that seemed to have a connection between all those injuries?
A. Yes. In this particular proceeding the product was OxyElite Pro so-called New Formulation which was introduced in 2013 and not too long thereafter a number -- a growing number of instances of acute, sometimes fatal, sometimes requiring liver transplant, so severe with injury I began to crop out in people who previously had been generally pretty healthy, I mean, they had -- they were often taking this because they were hoping to lose weight, so they were a bit obese but didn't have any recognized pre-existing serious heart, lung, kidney, liver disorder who developed this, as I said, sort of acute and sometimes serious, sometimes even fatal, liver injury.
Q. Is your method of analyzing this data that we were just discussing and drawing your conclusion consistent with how your peers would come to the same opinion?
A. Yes. I think so.

Q. And were the facts in the papers that you read, the medical records that you reviewed, the paper for the University of Arkansas about the animal study, was that enough for you to concern that OxyElite Pro New Formula is a risk to the public?

A. Yes.

Q. If one of your patients came to you and said, "Hey, Dr. Bonkovsky, I've got this bottle, this stuff called OxyElite Pro New Formula would you say go ahead?

A. I would strongly recommend that they not do so.

Q. Do you believe your testimony would be helpful in assisting a juror or a judge in understanding the facts in this case?

A. I believe so, yes.

MR. SULLIVAN: Your Honor, we previously filed Dr. Bonkovsky's CV with the Court. However in the last year it's been updated. I have an updated version I would like to substitute for that and I will just mark it as Government's Exhibit A. It was previously forwarded to the Defense last week.

MR. NIEWOEHNER: Yes.

MR. SULLIVAN: Your Honor, if I may enter that -- submit it for the record.

THE COURT: Hearing no objections, admitted.

(Admitted in Evidence as Government's Exhibit A.

MR. SULLIVAN: Thank you, Your Honor. Pursuant to Federal Rule of Evidence 702, I tender Dr. Bonkovsky as a qualified expert in the field of hepatology.

THE COURT: For the benefit of our record and the court reporter would you please just announce yourself each time a different person is at the microphone. We will have a cleaner record. I appreciate that.

MR. NIEWOEHNER: Thank you, Your Honor. Chris Niewoehner on behalf of USPLabs.

CROSS-EXAMINATION

BY MR. NIEWOEHNER:

Q. Dr. Bonkovsky, you have prepared an expert report or an expert notice in the course of this case. Is that correct?

A. Yes.

Q. In that report you acknowledge that you do not know why OxyElite Pro New Formula supposedly causes any injuries. Is that correct?

A. In the since of a detailed molecular pathogenesis, that is correct, yes.

Q. You can't explain the process, whether it's physiological or chemical, by which I'm going to call OEPNF. Do you understand what I'm referring to? You can't explain the process or the chemistry or the physiologics behind what injuries are occurring in these people and the substance. Is that correct?

A. That's correct.
Q. You also understand that OEPNF contains a substance called Aegeline?
A. Yes.
Q. You also do not know that Aegeline is the cause of an injury suffered by these people. Is that correct?
A. That's correct. I have thought all along that it was more likely a combination of the ingredients in OEPNF that was causative in the injury experience and I believe there are a number of other components in OEPNF like caffeine and Higenamine and a few others as well and so it seems more likely to me and I think the recent paper of Luis et.al. that appeared in I think it was student chemical toxicology have supported the idea that a combination of ingredients was potentially toxic, in fact, was toxic certainly to mice in some pretty standard studies of toxicology performed at the University of Arkansas Medical Sciences Center.
Q. So you agree with my question which is that you don't know that Aegeline is the cause of the injury; correct?
A. That's correct.
Q. Further, you are aware that there have been efforts to study whether OEPNF is evident hepatotoxic; correct?
A. Yes.
Q. What does it mean to be hepatotoxic?
A. It simply means that is something that leads to liver

damage, liver injury, so something toxic to the liver.
Q. You are aware that the government has done tests to determine whether OEPNF is hepatotoxic; correct?
A. I don't think it was the government itself. You mean -- My impression is that the laboratory is not per se a government lab, although it may and I think it did have some support from a contract with the Department of Justice.
Q. Well, the FDA -- maybe it wasn't a government lab per se, but you understand it was being done on the behest of the government; right?
A. Yes.
Q. And you understand that the testing was designed to look not just at the overall substance but also it's components; correct?
A. Yes.
Q. And you understand that this testing could not identify that either the substance or its components were, in fact, hepatotoxic; correct?
A. What was done was the material, this combination of several ingredients, and it appears they were all synthetic ingredients, not derived from natural sources, at least as evidenced by the analysis of Dr. Khan and his group at the University of Mississippi indicated that it caused death of mice, caused various other toxicity. Now, it was not designed to try to come up with the exact molecular mechanisms that

were leading to this death, so I take your point with respect to that. I would certainly not agree that these studies did not indicate that there was danger and toxicity to this combination of ingredients in OEPNF.

Q. Dr. Bonkovsky, this will go faster today if you can try and focus on my question. My question was: The testing doesn't show that OEPNF or its components was hepatotoxic. Is that correct?

MR. SULLIVAN: Your Honor, I just ask Mr. Niewoehner to clarify if he means the mouse study, if that's what he is talking about. He was talking about the testing. I just want to make sure we are on the same page.

BY MR. NIEWOEHNER:

Q. Let's for a moment -- I tell you what.

MR. NIEWOEHNER: Your Honor, if I may approach. There's a binder we put together of some exhibits we will use which we would give the witness, Your Honor.

THE COURT: Sure.

MR. NIEWOEHNER: How does Your Honor prefer, give it to the deputy or give to it the witness directly?

THE COURT: You can approach the witness.

BY MR. NIEWOEHNER:

Q. Dr. Bonkovsky, if you could, I would like you to turn to Tab 17. Do you see that?

MR. SULLIVAN: Your Honor, I'm going to object to any

question from Mr. Niewoehner that goes into the underlying facts. The underlying facts in this matter are a matter for the trier of fact in a trial and not in a *Daubert* hearing. So he is asking questions about Mr. Bonkovsky -- Dr. Bonkovsky's methodology. I understand that. But I'm going to object about any attempt to go into the underlying facts of Dr. Bonkovsky's review of the actual underlying facts in this matter. It's just not appropriate.

THE COURT: I guess I'm not sure yet what you mean by "underlying facts."

MR. SULLIVAN: Sure, Your Honor. The Fifth Circuit instructed us that this isn't supposed to be a trial. It's supposed to be a hearing on whether Dr. Bonkovsky is qualified, whether his methodology is sound and his opinions reliable that can help the jury to understand something because he isn't a layman.

THE COURT: Right. So I guess I'm just trying to determine at this point what he's planning to question him about has to do whether -- what his opinion is.

MR. SULLIVAN: Relative objection to anything about the underlaying --

THE COURT: It's hard to make a relative objection.

MR. SULLIVAN: I get you, Your Honor.

MR. NIEWOEHNER: Your Honor, at the moment I'm asking -- trying to figure out which studies he's looked at

and which ones he hasn't.

THE COURT: You may proceed.

BY MR. NIEWOEHNER:

Q. All right. I'm turning to what's been marked as Bonkovsky Cross Exhibit 17. If you will look at the top of the first page of that exhibit. You see it's a report on the In Vitro Hepatotoxicity Screening of Hawaii ORA Outbreak Samples of OxyElite Pro and Related Chemicals. It's by an individual by the name of Thomas Flynn and some other folks. If you look at the line underneath Thomas Flynn, it reflects he's a research chemist at the FDA/CFSAN. Do you see that?

A. Yes.

Q. Are you familiar with that study?

A. No.

Q. The Government has not shown you this report done by the FDA?

A. No.

Q. If you were to look at page 1 --

MR. SULLIVAN: Your Honor, I object. He has already said he has not seen this report.

THE COURT: Counsel, where are you going with this if this is not --

MR. NIEWOEHNER: We are allowed to test whether he has reviewed appropriate reports, if he has intentionally closed his eyes to relevant reports that would go to his

methodology.

THE COURT: Okay. You may proceed.

BY MR. NIEWOEHNER:

Q. Okay. I'm going to direct you to a sentence -- it's a little tricky to find, so tell me if I -- if you are struggling to find it. It's about 12 rows up from the bottom of the page. It's a sentence that says "neither simulated fatty litter. Just nod your head if you can find that part.

A. Yes. I see that sentence.

Q. It says, "Neither simulated fatty liver nor inflammation altered the cellular responses to OxyElite Pro in any way that would suggest enhanced liver toxicity. In summary, our assays reveal that no 'smoking gun' that would conclusively identify OxyElite Pro or any of its components as a liver toxicant." Do you see that?

A. Yes.

Q. So this study is purporting to show that neither OxyElite Pro or its components is hepatotoxic; correct?

A. Yes. Within the rather marked limits of the methodology used, I see that the systems included two human and one rat liver cell line and it's very well known these cell lines, for example, very rapidly use their normal compliment cycles before 50, these class of enzymes that are responsible for a wide variety of drug metabolism, and also these experimental systems do not include really any aspect of the immune system

of the animal and many of these injuries, particularly idiosyncratic injuries I was talking about earlier, involve very importantly immune responses to perhaps metabolites or toxins and the like. So, yes, within the -- within the pretty extreme limits of the methodology used.

I do notice that a little bit farther up, there's also a sentence that you chose not to highlight. Extracts of both -- Extracts of both OxyElite Pro capsule content and the Bauhinia pruriens extract, that's an herbal, showed some signs of cellular toxicity while Aegeline and Higenamine had only minimal effects on the cell.

Q. Dr. Bonkovsky, do you recall my original question?

A. No, I do not.

Q. I read you the line and asked you if that's what it said, essentially, and that the conclusion is that OxyElite Pro and it's components are effectively not liver the toxicants. Is that correct?

A. Yes. I already answered that.

Q. I'll ask you to -- Dr. Bonkovsky, are you familiar with a Dr. Ikhlas Khan from the University of Mississippi?

A. Yes.

Q. In fact, you've actually reached out to him in the past to help with an OEP study. Is that correct?

A. I might have. I can't remember, but it's possible.

Q. You're aware that Dr. Khan has testified as a Government

witness on behalf of the Government?
A. I wouldn't be surprised. I didn't know that particularly, but I wouldn't doubt that he had.
Q. May I direct your attention to Tab 12, please. There's Bonkovsky Cross Exhibit 12. It's a two page e-mail. Take a moment to familiarize yourself. It appears to be from yourself and Dr. Khan.
A. Yes.
Q. And I'll direct your attention to the second page of the exhibit. If you look at the very bottom, you will see an e-mail from yourself on 10-20-14 of 2:47. Do you see that?
A. Yes.
Q. You ask Dr. Khan, in the second line, "I wonder whether you or your team may have had occasion to perform analyses of OxyElite Pro," and you go on to say, "If so, are you able to share the results of your findings?" Do you see that?
A. Yes.
Q. And if you go to the top of the same page, the very top e-mail, there's one of 10-21-14 at 8:29 from yourself as well. Do you see that?
A. Yes.
Q. What you say, "What I'm working on right now is one case, one batch of OxyElite Pro. There might be more in the future. Subject of litigation versus USPLabs, Inc. Do you see that?
A. Yes.

Q. What were you seeking to get Dr. Khan's assistance with?
A. Trying to find out what was actually in the batch of OxyElite Pro. As I remember, this was a patient in Florida who had experienced an acute and severe liver injury after taking OEPNF.
Q. And why were you interested in that particular patient?
A. I had been asked to be an expert witness for the Plaintiff in that proceeding.
Q. Was --
A. I thought it would be important to know what was actually in this OEPNF, so that was the reason for reaching out to Dr. Khan.
Q. And the plaintiff, that was a litigation against USPLabs. Is that correct?
A. Yes.
Q. The person was suing USPLabs with respect to something to do with the OEP?
A. Yes.
Q. How many times have you worked with plaintiffs who are suing USPLabs?
A. To the best of my recollection, that's the only -- the only one.
Q. Were you paid for your work in that case?
A. Yes.
Q. How much were you paid?

A. My usual rate is $500 per hour for doing expert review.
Q. Did you prepare an expert report in that case?
A. Yes.
Q. What was the conclusion of that report?
A. Based upon my review of the entire record and history and so on, I thought that it was more likely than not that this particular person had experienced serious injury as a result of his taking OEPNF.
Q. Have you been consulted with other plaintiffs looking to sue in cases involving USPLabs's product?
A. No. Like I said, I don't think that I have been approached by others.
Q. And what was the name of the plaintiff?
A. I think the name last name was Rizzo, if I remember right.

MR. NIEWOEHNER: Your Honor --

THE WITNESS: R-I-Z-Z-O.

MR. NIEWOEHNER: Thank you. Your Honor, I'm going to note for the record that we haven't been provided with this expert report which appears to be on the exact same topic that Dr. Bonkovsky's report in this case is about. I presume it's available to the Government and so I will obviously continue, but we may be asking to reopen this subject to what we consider to be proper notice.

THE COURT: Do you have a response?

MR. SULLIVAN: Sure, Your Honor. That suit was

against USPLabs and these defendants that are here. They have that expert report. I don't believe we've ever seen that expert report. I don't think we have an expert report. We asked them for reciprocal discovery for all the civil cases from day one when we first turned over discovery to them in 2015 in December. To my understanding now, I don't believe they turned over a single document to us in discovery other than what they filed on the record or what we got from a subpoena they issued to someone who then sent us a copy also of what they sent to the defendants, so I assume that they have the expert reports from the USPLabs cases and all the plaintiffs that filed cases against USPLabs. So if Mr. Niewoehner doesn't have it, maybe he should talk to the lawyers who also represent USPLabs. I don't know, Your Honor.

THE COURT: In other words, you don't have it.

MR. SULLIVAN: I don't have it.

MR. NIEWOEHNER: Well, Your Honor, we'll note, of course, that just because Mr. Sullivan doesn't have it doesn't mean he doesn't have an obligation to obtain something which he can get from his own witness. We will also note that there's protective orders in the civil cases. It does not mean that I necessarily get access to those materials, so the Government can't simply assume that they don't have to comply with their duties because there's a civil case out there.

BY MR. NIEWOEHNER:

Q. All right. So I will look at -- I ask you to direct your attention to Exhibit 24.
A. I'm sorry. What --
Q. Exhibit or Tab 24. Excuse me. If you would look at Bonkovsky Cross Exhibit 24. It's an e-mail. You see that on the first page?
A. Now, is this the one that subject Old Miss DDSP Research Project Review?
Q. That's correct.
A. I see that.
Q. It's an e-mail. If you look down into the body of the e-mail you see there's a line that says, "All attached are a couple of reports from Ikhlas during my last visit to Ole Miss." Do you see that line?
A. Yes.
Q. And then if you go to the second page of the exhibit, you see there's something called an overview. And the left-hand column is something that says hepatotoxic studies?
A. Yes.
Q. And if you go down to 2.3 you see there's and entry for OxyElite Pro. Do you see that?
A. Yes.
Q. And then there's two references there. One is toxicity of OEP healthy mice and the second is toxicity of OEP in health compromised mice. Do you see that?

A. Yes.
Q. Was this the mouse study you were referring to earlier?
A. I have no idea.
Q. Okay. If you would turn to the second -- the third to last page of the exhibit. If you would look in the lower right-hand corner, it ends -- there's a number at the very bottom that ends in and at the end there's a number that ends in an 080.
A. Yes. I'm on that page.
Q. If you look about halfway down the page, 2.3 project 3 liver toxicity of OxyElite Pro in mice. Do you see that?
A. Yes.
Q. Another reference to study No. 1 and if you look at the top of the next page there's study No. 2. Do you see that?
A. Yes.
Q. Have you been provided with these studies?
A. I'm sorry?
Q. Have you been provided with these studies?
A. No. I don't think so. Well, I don't even know -- Where were these done?
Q. These are Dr. Khan's from Mississippi --
A. No. As I said, the only -- the only thing I have seen was the published work from -- Well, Dr. Khan was involved with that but, first off, there was this Dr. Maurice from -- I believe it's Little Rock.

Q. I'll direct you to the conclusion that's on the last page. Do you see that? About half way -- a third of the way down the page.
A. Yes.
Q. And if you read the second sentence or read the whole thing, if you wish, "In the surviving animals, both healthy and health compromised, where their enzyme levels did not show any change suggesting no association of liver toxicity with OEP." Do you see that line?
A. Yes.
Q. You were not provided this study by the Government. Is that correct?
A. That is correct.
Q. All right. You can close -- or you can for a moment. In the expert report you prepared -- there is a notice that was given to the Defense which purported to be -- I'll show it to you so you don't have to questions. If you will look at Tab 10. And if you look at the first page you see your name there in bold?
A. Yes.
Q. And then there's approximately, oh, I don't know, 8 or 10 pages or so of information about your opinions. Do you see that?
A. Yes.
Q. Did you help prepare this?

A. Yes.
Q. Did you review it before it was final?
A. Yes.
Q. Did you have a chance to make any changes you wanted to?
A. Yes.
Q. All right. And as a part of your report, I'm going to direct you to page 5 for a minute. And you see the first full paragraph. It's in the middle of the page.
A. Yes.
Q. About halfway down there's a sentence that begins Dr. Bonkovsky will testify that given this evidence as well as any OEPNF toxicological profile, the supplement should not be consumed by humans because of the risks associated with its use and the lack of evidence for its being of any benefit for any condition or being of any use in the treatment of any disease. Do you see that?
A. Yes.
Q. What is the basis of your expertise to assess whether a dietary supplement has any benefit for any condition?
A. I think that it's important that in particularly drugs and things that are maybe not being marketed as drugs but that are purported to be of benefit for weight loss or for increasing energy or for body building or the like should really best be subject to prospective randomized placebo controlled trials and that is still the highest standard for medical evidence

for drugs or chemicals in terms of their being beneficial. The testimonials that one can read in millions of copies on the internet these days and so on are not adequate evidence that these things are of any benefit or useful for the treatment of any disease and to the best of my knowledge OEPNF has never been subject to any properly done, properly respectively randomized trials to establish it is of any benefit whatever perhaps except to the manufactures who make a lot of profit from selling them.

Q. Maybe you don't perhaps follow my question completely. You're a doctor; correct?

A. Yes.

Q. You specialize -- You're a hepatologist; correct?

A. Yes.

Q. That is a specialist in, essentially, the liver; the liver and the diseases surrounding it; correct?

A. Yes.

Q. You have given your opinion as to how dietary supplements should be marketed and tested. Is that right?

A. Well, I just provided something. I haven't -- as I remember written on this, but I tried to summarize my views in my prior response.

Q. Do you view yourself as an expert on determining the benefits of weight loss dietary supplements?

A. I wouldn't say that I'm a card-carrying weight loss

person, but I consider myself to be a well-informed, thoughtful, well-read physician with a great deal of expertise in clinical trials and in adequate clinical trials and inadequate clinical trials. I reviewed hundreds of papers for journals of all kinds, so in that sense I think I am fully qualified to opinion on what the standard of evidence should be for making these claims of -- for these various herbals and dietary supplements.

Q. I'm asking a different question though. What is your expertise to determine the benefits of a dietary supplement focusing on weight loss?

A. Well, I think just answered that. I'm sorry. I think I think I told you. What else do you want?

Q. Well, you agree you've never written on this topic; correct?

A. Not a peer reviewed paper that I recall.

Q. How about a non-peer reviewed paper?

A. Oh, yes, I've certainly written other things and made my views known to people who have asked over the years and, of course, I talk to patients every day, every week in the clinic and I can just tell you that my general advice, particularly to people with liver disease, but really to anybody, is that they would be better off being very cautious about using these dietary supplements and herbals.

Another thing that we found from our running this

Liver Injury Network, which is something that's sponsored by the National Institutes of Health, for studying people who have experienced liver injury from drugs or herbals and things like that, is that in the analyses that we've done, around 300 of these now, these analogies were done by Dr. Khan's laboratory, we found that over 50% were mislabeled so that what was claimed to be in these preparations was not actually what was found in the preparations and they were erroneous pretty much equally in both senses, that is things that they claimed to be there weren't there and things that weren't listed were found to be in them, often prescription drugs. So, for example, drugs being marketed to increase libido and so on turned out to be spiked with Viagra, which is one example. Drugs for arthritis turned out to be spiked with --

THE COURT: I'm sorry. Are you talking about the New Formula?

THE WITNESS: No. I'm talking in more general terms.

THE COURT: You've lost me. I'm sorry.

THE WITNESS: I'm sorry.

THE COURT: Let me ask you this, because I'm understanding the basis of your opinion regarding the risks associated but I don't understand the basis of your opinion that there isn't any benefit. That's the part I'm not getting.

THE WITNESS: Yes. Well, again, there is -- as far

as I'm aware, there has been no prospective placebo controlled randomized trial to establish that there's any benefit whatever to OEPNF.

THE COURT: So you're not so much opining that there is no benefit but that there is no evidence of any benefit.

THE WITNESS: Correct. No adequate evidence. I'm sure that you can find all kinds of testimonials and so on, but that is not adequate scientific evidence.

BY MR. NIEWOEHNER:

Q. You do understand that in the United States there's no requirement that dietary supplements perform the kind of case -- the standard that you would suggest they should be held to?

A. Yes, I do understand that.

Q. You understand there's thousands of dietary supplements that don't meet the standard that you just set?

A. I do understand that.

Q. So you would agree at least it's the state of the law in the United States that your opinion is not shared by the regulators in the United States.

MR. SULLIVAN: I object to that. Speculative, number one. Number two, Dr. Bonkovsky has already agreed that there's not any requirement under the law that supplement companies do actually have placebo tests before they present their products to market. However, they do have to make sure

that it doesn't create an unreasonable or a significant risk to the market itself and I think Dr. Bonkovsky answered the questions that were asked before.

MR. NIEWOEHNER: Putting aside the suggestion from my friend over here, I think what's clear is that Dr. Bonkovsky has a view of what the only test that he will agree applies to this particular substance is the sort of test -- the control standard that he has out laid that is inconsistent with the law in the United States, inconsistent with the practice in the United States.

BY MR. NIEWOEHNER:

Q. So, Dr. Bonkovsky, you would agree that your opinion is in contrast to the law and practice in this country; correct?

A. Yes.

Q. Have you done -- What other work have you done to determine the benefit of OEPNF?

A. I have not done other work.

Q. And those things you could do. You could do a search for articles. Is that correct?

A. I have done some searches for articles. I could do more, yes. That would be in theory possible, of course, within the limits of time, energy, hours in the day and the like.

Q. You weren't asked to do a review of literature to look for the benefits of OEPNF, were you?

A. No. No, I was not.

Q. And you haven't done so; correct?
A. That's correct.
Q. You weren't asked to consult with any other physicians or specialists in the field to determine if there's any benefit to OEPNF. Is that correct?
A. That's correct.
Q. And you haven't done so; correct?
A. That's correct.
Q. All right. Let's turn to your report again. You have provided some opinions about the association between use of OEPNF and injuries to people's livers. Is that correct?
A. Yes.
Q. And according to your report, the two primary sources of information you have noted here were some articles that you reviewed and some review of patient documents. Is that right?
A. Yes.
Q. Now, I will ask you to turn to page 13 of your report and you see there's a list of the following materials you reviewed to prepare for this report. Is that correct?
A. Yes.
Q. You have mentioned the article today -- I apologize. I may not -- including toxicity for a Moisse or Moisse, something like that?
A. Yes. I think the spelling is M-O-I-S-S-E. I could be wrong about that.

Q. And is that article in this list?
A. No. That article appeared after I had prepared this, but I had received a briefing from Doctors Gourley and Clucherbosch who were co-authors in that paper which, as I remember, appeared in Food and Chemical Toxicology. I suspect you've seen that paper.
Q. Are there any other articles that you reviewed that don't appear on this list?
A. Yes, I think -- I think there probably are but I'm not sure I could give you the references at this moment. I would have to go back and look at PubMed and things hick that.

MR. NIEWOEHNER: Your Honor, I guess I would note again for the record to agree that Dr. Bonkovsky's opinion is based on something that's not here. There's been a failure by the Government to tell us what those articles are so we can object on that basis and I will ask that they supplement their disclosure.

THE COURT: Sounds like that would be appropriate.

MR. SULLIVAN: If we find the other articles he has reviewed, Your Honor, we will be happy to turn them over.

THE COURT: He is being pretty clear that he has reviewed other things that you've not listed, so --

MR. SULLIVAN: I've heard --

THE COURT: You need to do that.

MR. SULLIVAN: Yes, Your Honor. We will.

BY MR. NIEWOEHNER:

Q. How did you choose which articles you reviewed?

A. By -- Namely, I subscribe to a number of these articles. For example, one of the earlier reports, American Journal of Gastroenterology. That's the official work of the American College of Gastroenterology of which I'm a fellow, so I received that publication and became aware of that. I am a part of this U.S. Drug Induced Liver Injury Network. It's something that's been sponsored since 2003 by the National Institutes of Health, the NIH, designed to try to identify patients who have experienced injury due to drugs or herbals and to characterize them and to obtain serum and the DNA to try to do testing for markers and so on, follow these people in terms of prognosis. And so the Heydeman, et.al. paper that's listed there was a series of -- a total of seven cases of liver injury seen in the mainland of the U.S. Now, the initial cases that you may recall were from Hawaii. Those were reported by -- we observed cases in the U.S. as well, some of whom, if not all, made their way into the Drug Induced Liver Injury Network registry of patients and database and, as I said, they were reported by Heydeman and others. Then -- Let's see. What -- What else did you want to know?

Q. Well, I think you've answered my question sufficiently. If you could turn to page 5 of your report. Keep your attention on the middle, the full paragraph, the last sentence

of that. You see it reads: "Dr. Bonkovsky will testify to his review of published peer review research describing the OEPNF associated outbreak, including that OEPNF is the only medically and scientifically plausible explanation for many of the case reports contained in the literature." Do you see that?

A. Yes.

Q. Now, you said "many of the case reports." You did not say all of them; correct?

A. Yes.

Q. Which ones did you review that did not support your opinion?

A. I can't remember the details sufficiently now. I would have to go back to the original records, it's been some time, but my recollection is that some of them just lacked certain information that would be considered to be important to fully exclude alternative explanations, meaning general the diagnosis of drug induced liver injury is what we call a diagnosis of exclusion, so that one has to exclude the possibility that could the patient have had acute viral hepatitis, for example. One has to exclude the possibility that it was actually acetaminophen, that it was actually alcohol, that it was not something called ischemic hepatitis which implies that there was either low blood pressure or some critical lack of sufficient oxygenation to the liver. That

can also cause an acute liver injury and resemble what one sees with OEPNF. And so that -- Some of those were just not complete enough to have a more -- likely than not that OEPNF was the cause.

Q. To understand your methodology it would be important to you understand which cases you thought did fit and didn't fit, wouldn't you agree?

A. Yes.

MR. NIEWOEHNER: Your Honor, that information hasn't been provided by the Government to us. This hearing was known as to when it was going to be. It's precisely the kind of information we are entitled to know to test his methodology, as he just agreed, and so again I'm going to have to ask that the Government provide some information about which case reports support and which don't.

THE COURT: I'll take that under advisement.

BY MR. NIEWOEHNER:

Q. All right.

MR. RUNKLE: Your Honor, could I respond to that for one moment?

THE COURT: Yes.

MR. RUNKLE: Okay. Your Honor, Dr. Bonkovsky I believe reviewed case reports from papers, so they have that information. Dr. Bonkovsky also reviewed medical records, which they also have that information, and I don't believe

that the Government is obligated under Rule 16 to provide them with a document that lists every single patient record that Dr. Bonkovsky has considered. They have the information that he has considered, the factual information, and I don't believe there's really a basis for that challenge.

THE COURT: Is that the case, Doctor, that the case studies that you are referring to are all included in the list of papers that you reviewed?

THE WITNESS: Yes, with the exception of this *Rizzo v. USPLabs* where I served as an expert for the Plaintiff. To the best of my knowledge, that has never been published, that case. But again, I'm pretty sure you guys must have all those records.

MR. NIEWOEHNER: Your Honor, there's a difference between us having the case studies and understanding how Dr. Bonkovsky's methodology works. He has acknowledged it's important to understand his methodology to know --

THE COURT: I don't understand your objection. You have the basis of his opinion and he's explaining to you how he arrived at it. What is he supposed to do at this hearing, walk you through each case study?

MR. NIEWOEHNER: If he has identified some that don't and he gave a list of reasons why they might not, then -- I don't know which ones he thinks they are or aren't. I don't want to ask him about every single patient in every case study

to understand that in this --

THE COURT: And how is this going to meet the *Daubert* factor?

MR. NIEWOEHNER: Because if his methodology -- I will make up a case. Let's say there's a case -- as the Doctor has explained, there is a diagnosis of exclusion. You have to exclude all the other potential causes before you come to the conclusion that this is a drug induced liver injury. Let's say the doctor -- I'm not going to make up an example, it's extreme, but let's say there's a clear diagnosis of hepatitis A. It's in the records and let's say Dr. Bonkovsky said I just ignored that.

THE COURT: But he is not saying that. So what's going on?

MR. NIEWOEHNER: We don't know -- All right. So in my extreme example, we don't know of the something like 75 cases that are discussed in the case studies which ones he thinks support and which ones he don't.

THE COURT: I don't think that's proper in this hearing. I really don't. I think what you are challenging -- how you are challenging him or the challenge you are making to this point sounds like it goes to the weight of his opinion rather than the admissibility of it which is the issue here. I mean, he has told you that he has excluded something and the basis for that exclusion, so I don't understand why you think

it would be appropriate here to go through case-by-case how he came to that conclusion.

MR. NIEWOEHNER: Because to test his application of his methodology.

THE COURT: But the test that you are referring to sounds more like a test of the weight to be given to his opinion rather than whether he is qualified to give his opinion. Maybe I'm just not saying it in the way that is clear.

MR. NIEWOEHNER: Okay. I understand. I guess we made our objection. Your Honor has obviously noted it.

THE COURT: Okay.

MR. NIEWOEHNER: But there was a reference to the patient records, Your Honor.

THE COURT: Okay. Reference to his review of them.

MR. NIEWOEHNER: Correct. And I'm going to mark what is Exhibit 44, which is two big binders.

THE COURT: Okay.

MR. NIEWOEHNER: And -- If you can give that to -- I'll represent that reflects the patient records that is represented by the Government that have been -- in the world that might have been reviewed by Dr. Bonkovsky -- and I present that to you in part to note that the Government has refused to say which of those records he has found to be relevant to his opinion. They simply dumped the records on

us; it was 52 pages worth. We have asked for which records form the basis for Dr. Bonkovsky's opinions and we have been told, "We're not going to tell you that." I would ask -- I'm happy to sit here -- I'm not happy to, but we can. I can show the Doctor the 52 records and say did you look at this one? Did you look at that one? Did you look at that one. I submit that's a terrible use of your time and ours. We would ask that the Government simply provide us with a list of patient records that Dr. Bonkovsky actually considered.

THE COURT: Did you give to the Government -- Did you provide to Defense counsel records that you indicate were reviewed by Dr. Bonkovsky in terms to his arriving at his opinion that you intend to offer?

MR. RUNKLE: They have everything Dr. Bonkovsky considered.

THE COURT: Okay. Well then why are there some that he -- that there's a suggestion he didn't consider?

MR. RUNKLE: I don't understand. I feel like we're sort of far afield from *Daubert* here.

THE COURT: Is there's some reason to believe that he didn't consider those things he has already provided to you? I don't understand the negative of that.

MR. NIEWOEHNER: And if he's telling me he considered every single patient and did every single review, then the next question is which ones are significant? We are trying to

deal with --

THE COURT: You are trying to -- You are trying to cross-examine him about his opinion.

MR. NIEWOEHNER: Which is inevitably intertwined with which records he looked at and considered relevant --

THE COURT: This is not the proceeding for that. This proceeding is so that you can challenge his methodology, not the basis of his opinion; two different things in my mind and how he arrived at his opinion but not how he comes to this conclusion. I think there's a distinction there.

MR. NIEWOEHNER: And I'll --

THE COURT: Maybe I'm not --

MR. NIEWOEHNER: I'll suggest --

THE COURT: -- explaining it well.

MR. NIEWOEHNER: I think I understand Your Honor's point and perhaps what we're asking for is a combination of their duties under the expert notice rules and this hearing.

THE COURT: What they're saying is they've given you those and you're saying you have those, so what is the objection except that you want to ask him further about those?

MR. NIEWOEHNER: Getting dumped two huge binders of records and saying he looked at them is not meaningful notice either for the Court's file or for this hearing because unless we actually know which of the patient records he found significant, then we can't assess his methodology of reviewing

the patient records. You can describe it generically or I considered this factor and that factor, but until I understand how it applied to a given patient, we are unable to test his methodology.

THE COURT: In this hearing you cannot.

MR. NIEWOEHNER: Understood, Your Honor. Thank you.

BY MR. NIEWOEHNER:

Q. I will direct your attention to page 11. If you look at the bottom paragraph, not the full one, the one that begins: "Dr. Bonkovsky will also testify as to his review of patient medical records collected by the FDA. Dr. Bonkovsky will testify that although the records are sometimes fragmented and lacking in follow up information, his review of the patient's records largely confirms the conclusion reached by the physicians and other health care providers who concluded that OEPNF was strongly associated with and the most likely cause of their acute liver injury in the Summer/Fall of 2013." Do you see that, Doctor?

A. Yes.

Q. Again, I'm going to focus you on the word "largely." You said you reviewed patients record and largely confirm those conclusions; correct?

A. Yes.

Q. Which one didn't confirm those conclusions?

A. I can't give you any specifics. I would have to read

through those volumes. It's been months since -- since I did those reviews and I don't remember them.

Q. You weren't asked to do that review before today's hearing; correct?

A. Not -- not to repeat it, no.

Q. Not to refresh your memory as to which records you relied on and which ones you did not?

A. That's correct.

Q. What were the reasons that you did not rely on the patient records?

MR. SULLIVAN: Judge, I object. I don't understand the question.

THE WITNESS: I relied on the patient records.

MR. SULLIVAN: Dr. --

THE COURT: He is answering. Did you finish your answer?

A. Yes. I -- Did you get the answer? I relied on the -- on the records that I was provided and -- on the peer reviewed published papers that we've been talking about.

Q. Did you make an individual determination of each patient's records?

A. Yes.

Q. And you decided that you -- that some confirm the conclusions and some did not. Is that correct?

A. Some were more nearly complete and thus stronger evidence,

but as I remember, I didn't find any of these where it seemed more likely that something else was the cause of the liver injury. Now, you get into having to -- weighing all these factors, and we do this every day in the clinic, given the overall presentation, given what we know about patients and about responses to these various drugs and chemicals and alcohol and all the things we've been talking about, one reaches and one has to reach a conclusion about what is the more likely cause. You know, you can always say, "Oh, well, maybe there was some unknown virus that caused it that nobody can find." Well, yeah, that's possible, but it's not as likely because as in these particular cases OEPNF was actually the main and proximate cause of the liver injury that the patients experienced.

Q. I'm going to focus on a different line that you touched on a moment ago. The same part that we just read. You said you will testify that although the records are sometimes fragmented and lacking in follow-up information, you would agree that it is important for your analysis that the records be as complete as possible; correct?

A. Yes.

Q. You say that the records are sometimes fragmented and lacking in follow-up information. What do you mean?

A. Well, a common problem is that now a days medical records are disjointed, there's often an excessive amount of

repetition in which things are just copied from one note to the next with little new information. It can be very difficult to find key pieces of laboratory information, imaging studies, the pathology is buried somewhere, it's hard to find, so in that sense things seem to be fragmented and not well organized. I think it's fairly obvious the follow up information, if the patient dies, there's not going to be follow-up. If the patient doesn't return for visits, misses appointments, whatever, the follow-up will be less than complete.

Q. You would agree with the statement the importance of a thorough history in DILI, describing use liver injury, cannot be overemphasized; correct?

A. Yes.

Q. You also agree with the statement that an accurate history of medication exposure and onset in the course of liver biochemistry abnormality is crucial?

A. Yes.

Q. The patient records you reviewed in fact often did not have histories prior to March of 2013. Isn't that correct?

A. I can't remember.

Q. Do you --

A. I can't say.

Q. You don't --

A. I would have to read over all those volumes.

Q. You don't recall here sitting today how far back in time the history went?

MR. SULLIVAN: Your Honor, I'm going to object. He's going quite a bit far afield by going into the details of the patient records themselves instead of Dr. Bonkovsky's methodology or looking at --

THE COURT: I think he is asking that. He is just asking if he knows how far back they went. And I'm going to overrule the objection.

By MR. NIEWOEHNER:

Q. As part of your methodology you considered what tests were done in the medical records; correct?

A. Yes.

Q. You observed that many times not all the tests that you would consider appropriate were done. Isn't that correct?

A. Yes.

Q. And so you would agree if those underlying tests weren't done, you would have less confidence in your own assessment; correct?

A. Yes.

Q. And you would have less confidence in the assessment done by another physician, say, in one of the articles?

A. Yes.

Q. And, indeed for many, if not most of these patients, you did not have thorough medical records to work with. Is that

correct?
A. I don't know. I mean -- What do you mean by "thorough"? You know, there -- there are -- medical records are imperfect documents.
Q. Well --
A. Some are more imperfect than others.
Q. These are your words. Many of them are sometimes fragmented?
A. I already explained what that means.
Q. You touched on this, but again in terms of your methodology in assessing whether a particular substance caused a particular injury, you talked about this is a test of exclusion; correct?
A. Yes.
Q. You have to exclude the non-drug causes for an injury before you can come to a conclusion that the drug supplement caused injury; fair?
A. Yes.
Q. There is no test, blood test or a liver test or enzyme test, that you can run that will objectively just tell you that OEPNF caused a given liver injury. Is that fair?
A. That's correct.
Q. So in terms of the things you test for, you reviewed the medical records and the case articles to see what tests were conducted. Is that fair?

A. Yes.
Q. You would consider first line testing for hepatic cellular or mixed DILI to include testing for things like acute viral hepatitis?
A. Yes.
Q. That would include Hep A, Hep B, Hep C?
A. Yes.
Q. Would you include Hep E?
A. Yes. Now, Hepatitis E turns out to be actually endemic in the U.S. and when studies have been done it's turned out, for example, about 50% of all patients in the midwest of the U.S. have evidence of having been infected in the past with Hepatitis E. Back in 2013 really good, reliable testing for Hepatitis E was difficult, if not nearly impossible, to get in the U.S. It's still not perfect. I think it's better now than it was then. But at the time that I think the doctors in Hawaii and then, for that matter, us on the mainland in the Drug Induced Liver Injury Network, we are seeing these cases testing for acute Hepatitis E was certainly not a standard of care. We were trying to introduce it, but recognizing the limits of the currently available tests, and there are three main tests. So when one is testing for something called IgM antibodies which are antibodies that arise quickly after a new viral infection, IgG antibodies that arise months after the infection and then typically sit for years, and something

called HEV RNA, which is a test for the ribonucleic acid of the virus itself. And, as I say, the antibody tests that were best back in those years were done at Dr. Purcell's laboratory at the NIH. There was question about the accuracy of the commercially available tests.

The other thing about Hepatitis E is that when Bob Purcell and his group tested around 680 plus samples of people from another NIH consortium called the Acute Liver Failure Study Group, so these were people that had developed acute liver failure, severe hepatitis from some cause, they found that virtually none of them had evidence of acute Hepatitis E infection. I think there were a total of three that had some evidence, but the opinion of the investigators in that study as that even in those 3 out of over nearly 700, Hepatitis E was not the cause of the acute liver failure and another cause was more likely. So even when, you know, these tests come back positive for viral hepatitis, that doesn't necessarily mean that the cause of liver injury in that particular case was hepatitis. A common example of that is that the Hepatitis C infection is pretty prevalent in this country, chronic Hepatitis C. So people that get acute liver injury from INH or Augmentin or whatever cause may have an underlying Hepatitis C infection. The fact that somebody tests positive for antibody or even RNA for Hepatitis C doesn't necessarily therefore mean that the cause of the acute

injury that one is now observing in that patient is due to Hepatitis C. So all of these things have to be taken into context in the entire case summary and the case presentation.
Q. Let me just repeat my question for a moment. You agree that Hepatitis E should be first line testing?
A. Today I agree that should be part of testing. I'm not so sure that I would agree that at the time that these patients were presenting in 2013, five years ago, that certainly was not standard of care then. One could argue that, well, yeah, it should be done, but I've already pointed out the considerable limitations and defects that were systematic defects in those years and they are not entirely addressed even today. The commercial tests are not necessarily always reliable for Hepatitis E antibody, for example.
Q. You would agree that in addition to testing for acute viral hepatitis you would also want to see testing for such things as cytomegalovirus, CMV?
A. Yes.
Q. Ebstein-barr virus?
A. Yes.
Q. Acute herpes simplex virus?
A. Yes. Although, you know, the clinical presentation of acute herpes simplex virus is that the patient is on -- virtually on death's door, so the frequency in which acute HSV is actually found in these cases of people that have drug use

liver injury who are sort of walking around with jaundice and feeling nausea and loss of appetite is virtually zero. It just is not -- doesn't turn out to be an actual cause. You can always bring this up, you know, in -- create out all these strong -- in terms of what's actually going on with the patient, it's not --

Q. You would agree first line testing would include autoimmune hepatitis?

A. Yes.

Q. Or ANA SMA, AMA -- A few abbreviations?

A. Yes. The problem with ANA is that particularly among women who are kind of more prone to autoimmune phenomena and so on, 20 to 30 percent of women have a positive ANA. So finding ANA, it's a piece but it's not -- it certainly doesn't make the diagnosis or autoimmune hepatitis. Someone with muscle antibody is somewhat more helpful because it is somewhat more specific, but even there it is not in itself diagnostic and it's necessary to put the results of all of these tests together into an integrated whole, as I've tried to indicate, that's the methodology that we as hepatologist need to continue to use.

Q. You also agree that Wilson's disease should be considered?

A. Yes.

Q. You would also agree that the Budd-Chiari syndrome should be considered?

A. Yes.
Q. You'd also want to perform a tox screen; correct, to rule out potential causes like an acetaminophen overdose?
A. Yes.
Q. You need to exclude alcoholic liver disease as well; correct?
A. Yes.
Q. Why would you need to exclude alcoholic liver disease?
A. Excess alcohol continues to be a cause of liver injury and I've already said though that the -- sort of the signature of these OEPNF cases with transaminases in the thousands are not those of alcoholic -- even acute alcohol hepatitis.
Q. You'd also want to be aware of chronic conditions; correct?
A. Yes.
Q. Why would you want to be concerned about chronic conditions?
A. Well, if someone has an underlying chronic liver disease, it probably doesn't increase their risk of developing hepatotoxicity from a chemical, from OEPNF, from Augmentin, from INH, whatever. But if that were to occur, the outcomes would be likely to be more severe. As I think you can imagine, if someone has already an underlying cirrhosis, it's compromised the liver and has an additional insult of a drug induced liver injury, the prognosis is likely to be adverse

and worse than absent underlying liver disease.
Q. It would be difficult to assess whether a particular liver injury as a result of a chronic condition that preexisted or is a result of a potentially new injury; correct?
A. It might be, although in the majority of cases like somebody that has had chronic Hepatitis C for a number of years, these people just don't have sort of spontaneous out-of-the-blue severe flare-ups where there transaminases suddenly go from -- you know, maybe they're plodding along for years at 100 to 200 and suddenly it's 2,000 to 3,000. It would be more likely that there's something else that has occurred on top of the preexisting Hepatitis C. So again, it really depends upon the individual circumstances.
Q. I'm going to turn your attention to one of the articles that you mentioned which is the Heidemann article. Do you recall that?
A. Yes.
Q. That article was submitted on behalf of the Dillon investigators. Do you recall that?
A. Yes.
Q. You yourself are a Dillon investigator?
A. Yes.
Q. Dillon is an organization that's been in existence for over ten years? Fair enough?
A. We started in 2003.

Q. Is working on long term grants with the government; correct?
A. It's a cooperative agreement. It's not a grant. It's a U01 mechanism. I don't know if you are familiar with that, but it implies that there is an active participation among the NIDDK and the group of investigators.
Q. And the NIH funds either directly or indirectly some of the efforts that are being entered --
A. A great majority of the efforts are funded by NIDDK, the National Institute of Diabetes and Digestive and Kidney Diseases.
Q. Approximately how much money has been contributed to that effort by the government?
A. I think the yearly budget is probably been about 8 million over the last -- well, I think the first funding was in 2004 and it continues currently.
Q. With respect to the authors of the Heidemann paper, you are familiar with those individuals; correct?
A. Some of them. I don't know all of them.
Q. Were you involved at all in the publication of the Heidemann paper?
A. No.
Q. Now, that article is a case study; correct?
A. Yes.
Q. That relies on the anecdotal evidence of liver injury?

A. What do you mean by "anecdotal"?
Q. Well, it -- it was not an effort to do -- There's no control group in the study; correct?
A. That's correct.
Q. There was no effort to provide a statistical context for the significance of the number of cases that were studied. Is that correct?
A. That's correct.
Q. All the cases -- The article does not define -- attempts to define how many cases you might statistically expect to see of liver injury; correct?
A. That's correct. What essentially this was, in the Drug Induced Liver Injury Network, as I mentioned before, we -- when we hear about cases of possible drug induced liver injury, we seek to enroll them into a registry, essentially, and if the patients meet the basic inclusion criteria for a certain degree of severity and the like, we enroll them, we get their consent and so on, and then we collect clinical information, physical examination, and obtain both standard laboratory studies of the type that we've been talking about, exclude viral hepatitis and autoimmune hepatitis, autoimmune hepatitis, ischemic hepatitis, and so on and also obtain serum and DNA for ancillary studies, so trying to find new biomarkers that would be predictive or that will be associated with injury from a certain drug or class of drugs, biomarkers

that may indicate what the likely prognosis is, and particularly trying to find genetic predispositions, so are there certain genetic markers that will be associated with an increased risk of development of liver injury from Augmentin, say, or from flucloxacillin or whatever, and for comparison groups we use generally published full genome databases which are now available from the Library of Medicine and elsewhere.

Q. Do you know whether this Heidemann article was peer reviewed or not?

A. Yes, it was.

Q. Do you know who the reviewers were?

A. No.

Q. Peer reviewers, you understand as a general practice, aren't going to look at the underlying medical records that are cited in the article; correct?

A. That's correct.

Q. So the ability of a peer reviewer to say C if an error was made with respect to the underlying diagnosis is very limited; correct?

A. If important points of the type we were talking about were not included in the reports of these cases, the reviewer would certainly know that and an astute reviewer would point that out to the editor and the editorial board as a defect in the manuscript and that would influence the overall recommendation of the reviewer as to whether the reviewer recommends

acceptance or rejection.
Q. To give an example. If, for example, the article said that a person did not have a preexisting alcohol condition in the liver and in fact they did, that's not something a peer reviewer is going to be able to spot; correct?
A. That's correct.
Q. Peer reviewers are also not going to be able to spot problems if the underlying medical records that were being considered were incomplete in some way; correct?
A. Correct.
Q. They're also not going to be able to recognize if the medical records that being referenced are referenced accurately or not; correct?
A. Correct.
Q. In the context of this kind of case study, the peer review is relatively limited in terms of what they can spot in terms of problems with the underlying medical condition?
A. It certainly has limitations.
Q. Now, in terms of your opinion, with respect today you are only making opinions with respect to OEPNF as opposed to other products that USPLabs might make in the world; correct?
A. Correct.
Q. So to the degree a study not actually -- a case article is not addressing OEPNF, you should not be considering that particular case study; fair?

A. For purposes of this proceeding, yes, I would agree.
Q. Your own -- Did you attempt to review the medical records that you had access to compare them to the case reports contained in the articles that you read?
A. No. I don't think that I did a detailed exhaustive point-by-point check of medical records versus reports. As I remember, I -- it wasn't clear to me which of those cases might have been reported and which patient number it was.
Q. So, in effect, you were not able to independently assess the judgments made in the paper about the underlying medical conditions?
A. Correct.
Q. So to the degree that you relied on that, your opinion is only as good as the underlying people who -- the authors of the report; correct?
A. Yes. With respect to the -- For example, the Routman et.al. report and the Heidemann et.al. report.
Q. You would agree that if the underlying records are incomplete that affect the reliability of the results?
A. Yes.
Q. And thus the reliability of your opinion?
A. Yes.
Q. Similarly, if the underlying reports are not reported accurately, that would affect the reliability of yourself?
A. Yes.

Q. And, in turn, would affect your reliability; correct?
A. Yes.
Q. Essentially, if there's garbage in to those articles it is garbage out in terms of your opinion?
A. Yes.
Q. The challenges we've discussed about case studies in this Heidemann article, I think you've already said this but just to make sure, that would be equally equate able to the Johnston article that you relied upon; correct?
A. Yes.
Q. There was a letter to the editor by Riteman who you relied upon it; right?
A. Yes.
Q. That would be equally applicable to the Riteman letter; correct?
A. Yes.
Q. And there was another article sometimes referred to as the MMWR and usually referred to as -- Let -- You can find it faster than I can. I think it's cited as MMWR? Do you know which one I'm referring to?
A. Yes. I think in the fall of -- I think there was an initial report -- MMWR. Morbidity -- Morbidity and Mortality Weekly Reports. It's published by some branch of the government. I think it's the CDC. I could be wrong.
MR. NIEWOEHNER: Your Honor, may I have just one

moment?

THE COURT: Yes.

BY MR. NIEWOEHNER:

Q. Dr. Bonkovsky, I'm going to ask you to turn to Exhibit 23.

MR. SULLIVAN: I'm sorry?

MR. NIEWOEHNER: Exhibit 23. I'm sorry.

BY MR. NIEWOEHNER:

Q. Do you recognize this to be the Heidemann article you've been discussing?

A. Yes.

Q. If you turn to the fourth page of the article, you will see there's a table in it.

A. Yes. Table 1.

Q. And if you look at the line across the top it says Case 1, Case 2, Case 3 through Case 7; correct?

A. Yes.

Q. And that represents seven different individuals who were the focus of the article; correct?

A. Yes.

Q. And if you turn to Case 7 at the back or at the end of it, you see it reflects an individual who is 36 years old, who is male, Caucasian race, with a BMI of 25.0. Do you see that?

A. Yes.

Q. I'm going to turn your attention to Exhibit 1. Excuse me. And you see, if you look at the first page of Bonkovsky Cross

Exhibit 1, you see it's an e-mail, someone named David Kleiner; correct?

A. Yes.

Q. And if you --

A. It seems to have been addressed to Dr. --

Q. Yes. I apologize.

MR. SULLIVAN: Your Honor, I am going to be object. I believe this is a private document and I don't know why he's being questioned in public court about the document itself. Snipe we don't have that.

THE COURT: Tab 23. That's a private doctor?

MR. NIEWOEHNER: No. 1.

THE WITNESS: Tab 1.

THE COURT: I'm sorry. I was on the wrong page here.

MR. NIEWOEHNER: I'm sorry, Your Honor. Tab 1. Your Honor, this is a document we received by a FOIA request from the Government much as I guess they assume we have documents that are accessible to our client, we presumed that they have documents that are accessible to their client.

THE COURT: What is the objection?

MR. RUNKLE: Your Honor, the objection is no discovery has been provided. We don't have this document. It's not in our possession. This is a document that apparently is part of the National Institutes of Health which I don't have any ability to get this document. I know that

Mr. Niewoehner thinks that the Government has total knowledge of all these things, but none of these people are members of the prosecution team. We don't have this document and they haven't given us any discovery.

THE COURT: Okay. So what does that have to do with it's use for this hearing?

MR. RUNKLE: So what that has to do with the use for this hearing is that we haven't -- we have never seen this document before, so the idea is that -- I'm certain where we are going is that the root count scores were improperly changed or inflated and we -- there is no way for us to be able to respond to that without having seen this document before. And also, it's exactly what we were talking about earlier. This is a baseline fact problem. This is a problem with whether these root count were accurately reported in the paper. I would be willing to bet that's where he is going.

THE COURT: I overrule your objection on the basis that you have not been provided it in discovery. I don't know what kind of discovery it is that you would have been provided with, but I do sustain your objection as to it going to a matter of fact for the jury. Unless you're connecting with counsel, I believe you've gone down that road quite a bit, so if I could get you to explain to me how this challenges his expertise or his ability to offer these opinions that have been proffered.

MR. NIEWOEHNER: Your Honor, what I would proffer, Mr. Runkle is actually inaccurate in terms of what we are going to do here, but we would establish through this document, I just -- I pointed to Case 7 in the Heidemann article and we would match up, I would be able to demonstrate, I believe, that this witness, that there is evidence about Case 7 in the Heidemann article in this exhibit. We would go through -- What I propose to do is go through and look at some of the assessment that was done in the Heidemann article, the conclusions of the Heidemann article, and compare it to what you find --

THE COURT: Is this something he reviewed and he is basing his opinion on?

MR. NIEWOEHNER: I have -- I would have to ask Dr. Bonkovsky. I have no reason to believe --

THE COURT: Why don't we find that out because I have no reason for me to believe that's not the case and if that's not the case I will permit you to make a proffer of what it is you want to establish. I do think we are getting far afield of what it is we're here to do today.

BY MR. NIEWOEHNER:

Q. I will clarify. Dr. Bonkovsky, I believe you have seen this e-mail and attached to it are some case documentation. Have you seen this before today?

A. No.

MR. NIEWOEHNER: So, Your Honor, what I would proffer to do is I would show, for example -- I apologize. I would use a specific example in Exhibit 23, which is the Heidemann article, on page 3, and if you look at the top right-hand column in tab 23 on page 3, you see a sentence that says: "Only one patient was a moderate drinker, and none had a history of alcohol abuse or obvious risk factors for viral hepatitis." That's a conclusion of the article. I believe through questions we would demonstrate that is false and as we've established with Dr. Bonkovsky, if that is false, it is garbage in and garbage out, that his methodology of relying solely on the authors of the article to the underlying assessment of the diagnosis and medical records is flawed with respect to the Heidemann article and thus his methodology of relying on the Heidemann article is similarly flawed, so we would ask permission to walk through with the witness to make that demonstration.

THE COURT: I'm going to accept your proffer that's where you would take the witness and I am going to deny your request to actually go through that with the witness.

MR. NIEWOEHNER: And I'll just make an additional proffer just for the record. I understand your ruling. We would do this exercise -- I could do this exercise with many, if not most, of the case studies that are contained in the articles that Dr. Bonkovsky relies upon. We would demonstrate

that the underlying diagnoses were inaccurate, were based on incomplete information or inconsistent with the opinions of the authors in other contexts, the result of bias by the authors, and were otherwise unreliable and we would do that for each of the articles that Dr. Bonkovsky has cited as being that he has relied upon.

We would also do a similar exercise with respect to the medical records that Dr. Bonkovsky has said he has relied upon.

THE COURT: I think you are conflating reliability with correctness, as I've read in Rule 702, and the advisory committee note and -- but I accept your proffer. I understand what you are proffering, but I believe that that's what I consider is correct than reliability of in support of the evidence -- the evidence in support of his opinion, so --

MR. NIEWOEHNER: May I have just one moment?

THE COURT: Yes.

BY MR. NIEWOEHNER:

Q. Just one other thing, Dr. Bonkovsky. We discussed the patient records that you did review. You said that you largely or mostly, I can't recall that, but -- the word at this moment, confirmed the conclusion you saw from other -- others; correct?

A. Yes.

Q. You didn't recall today which patient records that you did

that confirm and which you didn't; correct?
A. Correct.
Q. When you were going through this did you make a list of them at some point?
A. I didn't make a summary list.
Q. Did you take notes about which ones did and which ones you didn't?
A. No.
Q. With respect to the case studies, similar issue. You said they largely corroborated what you had seen. Did you make any list of particular case studies that you found either did or didn't corroborate?
A. No.
Q. Did you take any notes on that topic?
A. No.
Q. Did you give any more reports on this topic to the Government?
A. I don't believe so.
Q. Written reports?
A. Only what we've been going over.

MR. NIEWOEHNER: Your Honor, I'll tender the witness to the other defendants.

THE COURT: We can go in the order --

MR. GIBSON: Your Honor, I have no questions.

THE COURT: Does anyone have questions? Any Defense

counsel have additional questions? In light of the fact I'm considering everything that happened here as to each defendants counsel.

MR. WEBSTER: As to Cyril Willson, Your Honor, no questions.

MR. SHEARIN: As to Kenneth Myles, no questions.

MR. ROPER: No questions.

THE COURT: Is there anyone else?

MR. HALL: No questions as to Mr. Patel.

THE COURT: Sorry?

MR. HALL: Patrick Hall. No questions as for Sitesh Patel.

THE COURT: Yes?

MR. MCMULLEN: Your Honor, Joe Steve McMullen. No questions for as to SK Laboratories.

THE COURT: Thank you. That's everyone, I believe. Is there is there any redirect?

MR. SULLIVAN: One second, Your Honor. I think I have one question, Your Honor.

REDIRECT EXAMINATION

BY MR. SULLIVAN:

Q. Dr. Bonkovsky, I think we might have done this in your direct, but I'll just ask one more time to make sure. Do hepatologists like you when reviewing information, do they rely on published peer review case reports for information

about dangerous substances?
A. Yes.
MR. SULLIVAN: Thank you.
THE COURT: Any recross as a result of that question?
MR. NIEWOEHNER: No, Your Honor. Thank you.
THE COURT: And you don't have to respond unless there is some recross. I don't hear further response. Doctor, you may step down.
Should we go ahead and hear any additional arguments and by "additional" I mean that you've not already presented in your brief, which I'm familiar with at this time; or should we go ahead and take the testimony of the other doctor who is present?
MR. NIEWOEHNER: Your Honor, we're happy to proceed with argument but we defer to your judgment.
THE COURT: I'm going to -- You know what they need to do.
MR. RUNKLE: I think the briefs have spilled enough information on this.
THE COURT: If they want to argue, I'm going to permit it. Do you want to go ahead and present your other witness on the other motion as well?
MR. RUNKLE: We are prepared to do that.
THE COURT: You do want to argue today?
MR. NIEWOEHNER: Yes, Your Honor

THE COURT: Okay. Why don't we go ahead and -- so that we can get him out of here and hear from the other witness.

MR. SULLIVAN: Your Honor, is Dr. Bonkovsky excused?

THE COURT: Unless either side has objection to it? Hearing no objection, yes, sir, you are excused.

MR. RUNKLE: Your Honor, the Government calls Dr. Karl Klontz.

DR. KARL KLONTZ, GOVERNMENT WITNESS, was sworn

DIRECT EXAMINATION

MR. SULLIVAN:

Q. Good morning, Dr. Klontz.

A. Good morning.

Q. Dr. Klontz, could you state and spell your name for the record, please?

A. Yes. Name is Karl Klontz; K-A-R-L middle initial C, K-L-O-N-T-Z.

Q. Dr. Klontz, what's your occupation?

A. I'm a medical doctor.

Q. Where do you work?

A. I work for the Food & Drug Administration, the Center for Food Safety and Applied Nutrition.

Q. What sure present title, Dr. Klontz?

A. With the FDA I'm called the Medical Officer/Epidemiologist.

Q. How long have you held that position?
A. Since 1989.
Q. Let's talk about your academic degree. What academic degrees do you hold?
A. I hold a Bachelor of Science, International Economics Georgetown University and then I went to medical school for MD, University of California San Francisco. Subsequently to that I got my masters in Public Health from the University of California Berkeley.
Q. And do you have any special training in epidemiology?
A. Yes. After medical school I did one year of internal medicine residency at UC Davis, University of California Davis, and then I entered a two year preventative -- general preventative medicine residency. That's a residency, Your Honor, that focuses on public health. Part of that, the first year of that residency was to go to Berkeley, they're made me get a masters in public health where I focused on epidemiology. The second year of the residency I worked at the California Department of Health services. Think of it as the state health of California where I did exclusive outbreak investigations. Subsequent to that, I went to the Center for Disease Control and Prevention where I did a two year I think of it as a post doc. It's called the Epidemic Intelligence Service. It's a highly competitive program where physicians do just outbreak investigations for two years. Think of it as

the Peace Corps of outbreak investigations, two years of very rigorous work. You keep a suitcase packed with you to go on an airplane to investigate outbreaks at any time. So that's in a nutshell my epidemiology training.

Q. Out outbreaks have you studied in your career?

A. Hundreds.

Q. And those outbreaks came from what general sources?

A. My main focus has been on food borne diseases. That's my career. 30 plus -- it's my 30th year at FDA. It's on food borne disease outbreaks. In addition, however, I have applied epidemiology to a number of other areas just as a -- as I was called to do so, liver injuries, for example, environmental health, even in sociologic kinds of outbreaks. In middle schools and elementary schools you have mass hysteria. It's now called mass echogenic illness. I've applied epidemiology tools across the board.

Q. And when you came to the FDA you had the same title that you have now?

A. Yes.

Q. Are you licensed in your field?

A. Yes. I'm licensed and board certified. Licensed in medicine. Board certified in preventative medicine.

Q. And how long have you been licensed?

A. Since the end of my internship. 1984. Licensed -- Board certified since 1987. I took the exam and passed.

Q. What generated -- What life experiences generated your interest in public health in epidemiology?
A. The reason I didn't do clinical medicine was because I grew up in a number of developing nations. My father was medical missionary in India and he joined the U.S. Foreign Service, so I grew in India, Nepal, Austria, Columbia, and I came to the United States for college and I saw health more on a population basis rather than a one-on-one clinical basis that's what led me to go into public health.
Q. Do you have an interest in developing nation?
A. Yes, I do. I go at least once a year to developing nations to either work in public health as in the Colony Center of Bangladesh or on my own. I put up solar panels in very remote villages in a number of the countries so they can have electricity.
Q. Now, if you could talk a little bit about the duties and functions of you position at FDA.
A. Yes. My main duties and functions at FDA are to investigate outbreaks. Now, that was particularly the case when I first came in 1989, fresh out of CDC. By the way, for the record I want to say between my training at CDC and coming to the FDA I spent one year directing the Infectious Disease Section for the State Health Department in Florida. So at FDA my main functions have been outbreak investigations, assessing the adequacy of data the FDA requires before it pulls the

trigger and it says that vehicle has caused that outbreak. I have been probably one of the most key people at FDA over 30 years to do that, day-in-and-day-out.

Q. Have you done any teaching or lecturing in the field of epidemiology?

A. Yes. For 15 years I was adjunct facility at the School of Public Health at George Washington University where I taught epidemiology, began as an adjunct and all the way up to full professor.

Q. Have you written publications in your field?

A. I currently have approximately 75-76 peer reviewed publications in epidemiology and some book chapters as well.

Q. How many of those are about outbreaks?

A. Probably a third to half are about outbreaks. A number of others are in case series which in and of itself may not be an outbreak but certainly are compilations of cases, so the majority are related to diseases themselves or the outbreaks of them.

Q. And have any of your papers won awards?

A. Yes. I published a paper on Hepatitis A outbreak in Florida that won an award.

Q. Dr. Klontz, could you tell us -- Could you give us a general background about what epidemiology is?

A. Epidemiology is the study of the causes and the distribution of diseases and the factors that lead certain

people to get them and other not to. In a nutshell that's what epidemiology is.

Q. Are there different branches of epidemiology?

A. Oh, yes. There are a number of branches of epidemiology. Infectious disease is one I concentrate on. Under that food borne diseases is another subbranch. And then you've got environmental health, internal child health. There are a number of different branches of epidemiology.

Q. Now, turning your attention to the Fall of 2013. Did a potential outbreak involving a dietary supplement come to your attention at that point?

A. Yes. And in the Fall of 2013, just to refresh everybody's memory, the U.S. Government was shut down. Congress shut down the Government October 1 through October 16. On about the second day I was called back to work. I had an exemption for the furlough is how the bureaucratese goes. Come back to work because we have received at the FDA at that time -- at that time it was 21 medical records from the State of Hawaii that appeared to have, according to Hawaii officials, a strong connection between ingestion of OxyElite Pro or some other dietary supplement, which is case a definition I am sure we will get into, was broader than just OEP that needed to be evaluated. Those medical records had to be evaluated and I was the person called in to do so.

Q. Now, did you form a conclusion at some point about whether

OxyElite Pro New Formula was related to that epidemic?
A. Yes. As I reviewed the medical records, I found that there was, from my standpoint, a sufficiently strong connection between OxyElite Pro ingestion and the liver disease that was described in these medical records.
Q. Do you need a drink?
A. Yeah, I do.
THE COURT: Do they have water?
THE WITNESS: Thank you.
BY MR. RUNKLE:
Q. So what materials did you review to form that conclusion?
A. Initially, I reviewed the medal records that Hawaii had sent us. I was concerned enough at that point that I then said to my colleagues, "We need to look at our own records in FDA," MedWatch reports in particular, and MedWatch reports are essentially FDA's surveillance mechanism for adverse events and so I looked at those reports and it turned out we had 114 MedWatch reports in which a box down at the bottom of the MedWatch report that says "suspect product" was filled in OxyElite Pro and so I evaluated those 114 MedWatch reports.
Q. And how did you reach a conclusion based on your review of those reports? What was your methodology?
A. My methodology was with a background of what I had read in the medical records from Hawaii I then ascertained details from the MedWatch reports to see whether they were consistent

with the disease relationship with OxyElite Pro and the medical records in Hawaii was repeated in the medical records -- excuse me -- in the MedWatch reports and I was sufficiently satisfied, "convinced" is a better word, that they were.

Q. Is that a methodology that epidemiologist employ to identify the suspected cause of outbreaks?

A. Yes. In many instances it is. If there is a surveillance mechanism that has a standard form such as hepatitis the CDC uses, measles, one who routinely reviews those case forms to see the completeness of data and the biological plausibility. Let me put it -- what's being put on these forms makes sense he epidemiologically. If that's a standard tool we use in epidemiology, outbreak investigations.

Q. So in one sense, when you read these reports you relied on your experience in epidemiology to determine that OxyElite Pro was highly likely to be associated with this outbreak?

A. Yes. That's correct.

Q. Now, there are two branches of epidemiology or there are two types of epidemiology that I want to talk about. If you could describe the difference between descriptive epidemiology and analytic epidemiology.

A. Descriptive epidemiology and analytic epidemiology are the -- Let me just take another sip here. Those are the two branches, the two major tools when it comes to outbreak

investigations. The first one describes the time, place, person of individuals who are ill, descriptive epidemiology and then one, if necessary, goes on to an analytical mode where you actually do some statistical tests. You take a class of people, a group of ill people and a group of well people, and you ask them the same kind of exposure questions and run statistics on them.

Q. Is analytic epidemiology always necessary to determine the highly likely cause of outbreak?

A. In my 35 of years of experience I have relied an analytic epidemiology a good deal. I've run an number of case control studies, also cohort studies moving prospectively in time. But there are situations where the data from descriptive studies is compelling enough, particularly when the public health is at risk, that one can act, in my opinion, without doing an analytic study. As we speak, analytic studies are becoming harder and harder to do in the United States because land lines are going away. People don't want to answer cell phones from investigators from the government who want to ask well people a long list of questions. As a result, we in the FDA are having to use to use more creative mechanisms instead of running analytic studies, the CDC particularly. It's the CDC that does most of it the actual epidemiologic studies. We review them. That's the function of my 35 years was to review the CDC's work. The creativity is as follows: Trace backs

are increasingly being used. Since we can't talk to well people as easily, we expend a lot of effort trying to find whether there is a common source of a product that people are saying they are taking. If there's a common source that makes you very suspicious that that's the potential vehicle about the disease. That's was the case right off-the-bat with OxyElite Pro.

Q. So was an analytic study necessary to determine that OxyElite Pro was associated with this outbreak?

A. I did not as an epidemiologist, and I will stand by this, I did not think that an analytic study was necessary when the compelling amount of exposure to OxyElite Pro. It was there in the medical records and it was there in the MedWatch.

Q. What happened after you made that identification in October?

A. After I made that identification, working with others in the FDA, of course, the consensus was clear, was a clear one, moving all the way up to the Commissioner's level. At this point, confronted with the risk, OxyElite had to come off the market and so that was -- that was my feeling. I was probably one of the main advocates of that.

Q. What happened after it came off the market?

A. This outbreak ended abruptly. This reminds me of essentially John Snow's work on cholera in London in the 1800s when we had a cholera outbreak in London and he found out that

people were getting water from the same pump. That was the common exposure. He took the handle off the pump and the outbreak ended. I think that's a fair analogy here.

Q. Have there been other outbreaks where FDA identified the wrong cause for an outbreak?

A. Yes. I would say there have been situations where the CDC plus the FDA, we work hand-in-glove, have got it wrong. Not many of them. Not many of them. One though I would like to bring to your attention was 2008. A large outbreak of salmonella saintpaul infections. The CDC and the FDA, after a lot of work, including analytic studies by the way, said it's tomatoes, tomatoes was causing the outbreak. And the tomato industry took a hit in 2008; yet the outbreak continued unabated. More work by the CDC and FDA. A couple of weeks later CDC calls us up and says it's hot peppers, jalapenos and serrano peppers, and that was exactly right. The media went out, said folks be careful about eating jalapeno and serranos; outbreak ended. You can get it wrong. You can get it wrong even when you do analytic studies.

Q. Did you get it wrong in this case?

A. I don't believe we got it wrong in this case. We had an abrupt increase in hepatitis unspecified causes that had its onset in the summer of 2003, built up as time went on, and then we in November announced a recall, the company and FDA, and that outbreak ended.

Q. Dr. Klontz, what is stimulated reporting?
A. Stimulated reporting is a term used for media, essentially, letting the public know that there is a relationship and an exposure of a disease and you need to know about that and that gets -- of course it goes to physicians as well -- and that increases the number of reports to regulatory agencies.
Q. Is stimulating reporting a bad pain?
A. No, stimulating -- stimulating reporting is actually can be a very good thing. If you are going to understand as scientists the relationship potentially between an exposure and an outcome you want to know more about what cases exist out there, so it's a very important role for both consumers and scientists.
Q. And in this case what you found after the news reports went out was that there were additional cases where the date of onset of injury was prior to the stimulated report. Is that right?
A. That's the key. That's the key finding is that stimulated reporting led to more reports that came to FDA and in those reports it showed that the timing of onset of illness pre-dated sometimes by months the media, and that's a critical finding here. When the people got sick it was not affected by media. It was affected by when they started taking OxyElite Pro.

Q. And did the -- Did the uptake in OxyElite Pro related injuries come in association with the release of OxyElite Pro New Formula, in your opinion?

A. It appeared to. Well, looking at MedWatch again and the medical records, but I'm going to focus on MedWatch here in particular and I want to be really specific on the numbers of MedWatch reports. 114 reports total reporting illness from January 2011 to February of 2014. We received 114 reports. When I looked at each one of those, I divided those into two categories: Those reports that documented liver disease of unrelated mediology. They didn't have infectious disease. They didn't have autoimmune hepatitis. They didn't take -- go overboard with acetaminophen or alcohol. When those were ruled out, those went into a group called -- I call -- Those that didn't have a liver disease due to specific known causes were categorized as liver disease likely due to OxyElite Pro.

Of those 55, we had information on the dietary ingredients of OxyElite Pro that were taken by these individuals for ten individuals. One of those people said they took DMAA containing OxyElite Pro. Eight said they took aegeline containing OxyElite Pro. One took OxyElite Pro a sufficient amount of time -- actually took both the DMAA at one point and then aegeline at another point.

THE COURT: When you are talking about OxyElite Pro, are you talking about the New Formula?

THE WITNESS: Well, what I'm getting at is the fact that in 9 out of 10 individuals who reported the type of OxyElite Pro they took before they became said it had aegeline in it. I'm assuming that's the new formulation.

Q. Dr. Klontz, what are the Bradford Hill factors?

A. Bradford Hill factors are a number of factors that have to do with causality, biological plausibilities, pluralities, and so on.

Q. Are the Bradford Hill factors necessary to do epidemiology?

A. I think it's important as epidemiologies always to be mindful of the Bradford Hill criteria. They are important criteria. You always want to have them in the back of your mind. In fact, you reflectively, instinctively are testing what you read and learn to those criteria. They are exceedingly important criteria. When you are in a public health situation, a nation of 330 million people, and you are convinced that a product is the cause of an ongoing outbreak, you may not be able to meet all of the Bradford Hill criteria. But, nonetheless, with OxyElite Pro, several of them were met, in my opinion, so I was -- we were mindful of them.

Q. And did you conform your findings about OxyElite Pro to toe some kind of FDA line that was forced on you?

A. Never. I will speak to that. I saw that. I saw that argument. Your Honor, if I may say, I have a reputation of

being a very independent minded person at FDA. I don't toe the line. I went into public health because I believe in the importance of public health, not in lines being towed. I feel very strongly about that.

Q. Do you believe that your testimony will be helpful in assisting the judge or a juror understanding the facts in this case?

A. Well, I'm -- I -- I believe the -- What we learn from the MedWatch reports is very significant and it does elicit some key, temporal findings that can explain the relationship between exposure to OEPNF and the disease.

MR. RUNKLE: Your Honor, pursuant to Federal Rule of Evidence 702 I would tender Dr. Klontz as an expert in epidemiology.

MR. LINEHAN: Good morning Your Honor. Good to see you again. Patrick Linehan on behalf of USPLabs.

CROSS-EXAMINATION

BY MR. LINEHAN:

Q. Good morning, Dr. Klontz.

A. Good morning.

Q. Let's just -- I just want to make sure I understand the scope of the effect of your expert opinion that you're proposing here. Your proffered area of expertise is in the area of epidemiology?

A. Correct.

Q. You're not a hepatologist?
A. No.
Q. I know you have an MD. Do you have a clinical practice?
A. I do not have a clinical practice.
Q. When was the last time you actually saw a patient?
A. I was sort of moonlighting during my preventive medicine residency in the mid 80s the last time I did a clinical practice.
Q. Do you recall treating any liver patients?
A. Yes.
Q. In the mid 80s?
A. Yes.
Q. No -- Nothing more recent than that though?
A. Not treating no.
Q. So you -- You're not offering an opinion based on any expertise in hepatology?
A. Not on hepatology, per se as a subspecialty of internal medicine.
Q. You are not an expert on dietary supplements?
A. I've dealt with a fair number of dietary supplements in my 30 years at FDA. For example, upon arriving at FDA in 1989 there was a massive outbreak of Eosinophilia-myalgia syndrome. It's called EMS. It was due to L-Tryptophan, a dietary supplement. I was involved in that. One clock forward, Hydroxycut, 2009. I co-hosted a paper with a number of

academic physicians on an outbreak of liver disease in Hydroxycut and now -- Oh, I've also published a paper on hypervitaminosis D and now OxyElite Pro.

Q. But in your -- Your disclosure doesn't indicate that you are offering any expert opinion on dietary supplements generally. Is that inaccurate?

A. Which disclosure --

Q. Let me put that in front of you. In fact, maybe we can get -- find our exhibits. While we do that, Dr. Klontz, you say you have felt dealt with a number of outbreaks -- I'm sorry. Can you give me that number again, just a range.

A. Outbreaks in general?

Q. Outbreak investigations.

A. Hundreds.

Q. Hundreds.

A. Hundreds.

Q. How many of those involved dietary supplements?

A. I would say probably 20 to 30.

Q. Okay. Let's turn to Tab 29 in the binder.

A. Okay.

Q. Have you seen this document before?

A. Yes. Yes.

Q. There's no indication that you're offering an expert opinion on dietary supplements. Is that a fair characterization of the document?

A. That's a fair characterization. However, let me remind you that the epidemiologic tools apply to dietary supplements, as I mentioned --

Q. I understand. But you are not dietary supplement expert. You are a epidemiologist.

A. An epidemiologist is experienced in some outbreaks of dietary supplements.

Q. 20 out 100s?

A. 20 to 30, uh-huh.

Q. You've not done any analysis as to whether OEPNF offers any benefits to those who consume it, have you?

A. I have not done an analysis of that, no.

Q. Now, according to your -- According to your disclosure, your opinion that you will be offering in trial is that based on the epidemiological evidence collected from a review of patient records and from MedWatch reports submitted to FDA OEPNF was strongly associated with and most likely responsible for liver disease among 55 patients that you discussed?

A. Correct.

Q. Do you have any other opinions -- other opinions that you -- that you plan to offer?

A. That's my central one.

Q. Let's talk about the materials you've reapplied upon. All right. We received files that cover 52 patients. I'll represent that to you. There are 55 patients that you've been

talking about. Is that -- Do I have that number right? 55?
A. 55 is the number of MedWatch reports, yes, that went into my study that was published.
Q. And did you review the underlying patient records -- any patient records that were associated with those MedWatch reports?
A. Yes. In some instances I did. There was a handful where I thought that the MedWatch report indicated the disease severe enough that I wanted to corroborate by medical records if we could track these patients down and get permission we did so.
Q. To your recollection, with respect to the 55 patients, you had either a MedWatch report or a MedWatch report and underlying patient records for each of those 55 patients?
A. That's correct.
MR. LINEHAN: Your Honor, I would like to note for the records here we have records only for the 52 of the 55. We would request those records -- that those additional records be provided.
THE COURT: I know you had said before you had 47. Have any given you more since then? I think in something I've read you had only 47 --
MR. LINEMAN: Well, the 47 may refer to those where underlying patient records have been provided; the rest being only MedWatch reports.

THE COURT: Okay.

MR. LINEHAN: So we -- So if there are -- If there are underlying patient records for the four MedWatch reports that we -- the four which patient records were not provided, then we would want those patient records to the extent that Dr. Klontz reviewed those, but there were also three patients where we received nothing, assuming that the 55 patients in Dr. Klontz's testimony is actually 55 patients. We only have any record at all for 52 of them.

THE COURT: Have you provided --

MR. RUNKLE: Your Honor, there's a confusion going on about different sets of information. There are MedWatch reports and then there are patient records. Only a few of those patient records actually intersect with the set of MedWatch reports, so I don't understand exactly what the question is. I believe everything has been turned over --

THE COURT: How many of those intersect what they have?

MR. RUNKLE: I think he should do this in his examination. It's something -- I mean, I'm not testifying --

MR. LINEHAN: So there are -- I agree with that.

BY MR. LINEMAN:

Q. So there are 55 patients that you identified out of the 114 adverse event reports you considered.

A. Yes. Let me back up and try to provide some

clarification. On the two worlds of records here, as I mentioned earlier, when I first was called on to go back to FDA to work, it was to review the medical records submitted by the State of Hawaii. In the end, by the end of this investigation, months forward, 46 records were submitted to FDA. The medical records were submitted by Hawaii to the FDA. Only those medical records met their case definition, the Hawaii case definition. Of those 40, 27 reported OxyElite Pro prior to onset of illness. That's one set records.

Q. So of the 55, 27 of those --

A. No. As to the medical records, the numbers I gave you 46, 40 to 27. Now we turn to the MedWatch world of reports, a completely separate entity. A surveillance system run by FDA in which we had 114 records to start with and I pared it down to 55 that I concluded that this was hepatitis of unknown etiology, likely due to OxyElite Pro. 55 Med records.

Q. There are 55 in the second bucket and how many in the first bucket?

A. Well, big world would be 46.

Q. 46.

A. I don't know how you want to define that first medical record --

Q. Is there any overlap between the 46 and the 55?

A. Yes. Some of the Hawaii patients who had medical records that were submitted to us did send in MedWatch reports. A

handful. That was one of our pushes at FDA. It's one thing to give us medical records, but we want to see MedWatch reports, too. We are always pushing to see MedWatch reports. There was some overlap there.

Q. Okay.

A. Just to be clear, in the MedWatch, as I said earlier, there was some proactive work we did as an agency to go out and get medical records for select MedWatch reports. That's another category of medical records. 5, 6, or 7 of those.

Q. Okay. So, let me just try and make this simple. There are 55 patients in your study on which your opinion is based?

A. My published study 55 MedWatch reports, yes.

Q. Some of which you have received underlying medical records for?

A. Correct.

Q. And others which you only have MedWatch reports for?

A. That's right.

MR. LINEHAN: Okay. So, Your Honor, my representation here is that we have either MedWatch reports or patient records for only 52 of those 55. And would like the other 3 -- To the extent -- to the extent Dr. Klontz has reviewed them, we would like the 3 -- the records for the other 3 patients.

MR. RUNKLE: I apologize for asking a question, Your Honor, but how many MedWatch reports total do you have in the

discovery?

MR. LINEHAN: So we have 4 -- we have 4 patients for whom there are only MedWatch reports.

MR. RUNKLE: That's not the question. We need know how many they have. We have turned over all of what we have and so it would be very surprising --

THE COURT: If you have turned over all of what you have I guess the question is, is that all he relied on. Do you have an obligation to turn over more. That's my given understanding.

MR. RUNKLE: I'm asking Mr. Linehan how many MedWatch -- Like, if there was failure to obtain MedWatch reports, it would have been an unintentional failure. We've obtained all the documents from the CORE team that reviewed these MedWatch reports of which Dr. Klontz --

THE COURT: Why don't you all after you leave here today get together and figure out what you've turned over and what they think they don't have and bring that all back.

MR. RUNKLE: We will do so, Your Honor.

BY MR. LINEHAN:

Q. And I just want to -- You said something I just want to make sure I understand. In the first bucket, the 40 patients for which you received patient files from Hawaii, that's part of 55?

A. Some of those patients in the Hawaii -- We narrowed it

down to 27 with OxyElite Pro.
Q. Okay.
A. Some of those 27 we do have MedWatch reports for; correct.
Q. So MedWatch reports and in some cases patient files?
A. Correct.
Q. So those 27 are part of the 55?
A. Substantive of the 27. Four or five of them we do have MedWatch reports for.
Q. Okay. Okay. Understood. Thank you.
THE COURT: What's contained in a MedWatch report? I mean, what is it that you are reviewing?
THE WITNESS: A MedWatch report is about two pages in length. It begins with some demographic factors, age, race, sex, gender, etc., then it goes into a sort of description of the event, a short box says what happened, what are you reporting. Usually, that's an illness kind of description. The bottom of that column is suspect product and that was how we can identify the 114 OxyElite Pro. The form then goes on to talk about whether the medications were taken, duration the agent was taken, what are the comorbidities, the health factors present, who reported the form, and -- Those are essentially the things. It's a -- It's a fairly brief form but filled out correctly provides enormously helpful information.
Q. And filled out incorrectly it provides not so helpful

information. Fair point?
A. You always have to be mindful of incompleteness or information that doesn't make sense. That's true all the time. You just -- That's the day-to-day practice of evaluating MedWatch reports.
Q. All right. So let me get back to the materials you reviewed in forming your opinion. We have the patient files, and I won't belabor the point, but the patient files plus the MedWatch reports. Do you have -- Aside from the MedWatch reports for the 55, where -- do you have a file for the rest of the MedWatch reports for patients that didn't make the 55?
A. Yes. Yes.
MR. LINEHAN: We have not received those, either, for the record, Your Honor.
BY MR. LINEHAN:
Q. You also mentioned you reviewed the expert reports from the plaintiffs and defendants in the Waikiki litigation.
A. Where -- Where are you showing that?
Q. So if you look at the last page of your -- the last page of your disclosure.
A. Uh-huh?
Q. Talks about your CV. Reviewed documents collected by the CORE team in performing this work and preparing this work as well as expert reports prepared by the plaintiffs and defendants in the Waikiki versus USPLabs case.

A. I'm trying to think of what that would be. I reviewed medical records. That -- that's it. Medical records.

THE COURT: Are you saying you reviewed medical records in those cases you didn't have actually records? Are you talking about MedWatch reports?

THE WITNESS: Yes. MedWatch reports are two page summary of an illness that is part of a FDA surveillance system.

THE COURT: But it's not a medical record?

THE WITNESS: No. That's to be distinguished from an a medical record which is generated by a physician in a hospital or a visit to his or her office or an ER.

THE COURT: So when you are testifying here that you relied on and reviewed medical records, are you talking about those MedWatch reports, too?

THE WITNESS: We really need to distinguish those two. When I say I reviewed medical records, those are hospital generated or doctor's office generated reports.

THE COURT: How many of those did you review?

THE WITNESS: From the state of Hawaii I reviewed 27, because they all said they had OxyElite Pro exposure.

THE COURT: Sorry.

MR. LINEHAN: That's okay, Your Honor.

BY MR. LINEHAN:

Q. So you did not review the expert reports from the Waikiki

case.
A. Define what you mean by an "expert report."
Q. Well, in litigation, parties hire experts to testify to provide expert testimony in their case and to give notice as to what that expert is going to testify, experts write reports.
A. I don't recall reviewing, when you define it that way.
Q. Any other materials you relied upon besides the MedWatch reports and the patient records?
A. Those are the crux.
Q. When you say the "crux" --
A. Let's say that was the totality of my review that led to my recommendation.
Q. And your disclosure also incorporates by reference an article that you wrote in 2015, or co-wrote in 2015 published in Public Health Reports. Do you remember that? Do you remember publishing an article around that time?
A. That's the article that summarizes the MedWatch reports, yes. I remember that.
Q. And it's been incorporated. I'll represent to you it's been incorporated by reference. I assume you stand by what's in the report?
A. Yes.
Q. Did you review the -- I want to be clear. Did you review the disclosure prior to testifying today, the disclosure we've

been talking about, Klontz 29.
A. Prior to today, no, I did not.
Q. Have you ever reviewed it?
A. Yes. When it was first written, yes.
Q. And aside from the representation that you had reviewed the expert reports in the Waikiki case, is there anything inaccurate about what's in this disclosure?
A. No. No. I would say no.
Q. Now, Dr. Klontz, you've testified today to some extent, and certainly in your disclosure, about two sets of tools used in epidemiological studies?
A. Yes.
Q. That's descriptive epidemiology and analytic epidemiology. In disclosure you say descriptive epidemiology, that epidemiologist essentially describe illnesses in terms of time, place, person and these so-called descriptive epidemiological features often provide clues as to the cause of illness. Correct statement?
A. Yes.
Q. With respect to analytic epidemiology you say that statistics and other mathematical assessments are applied to ascertain specific factors associated with these?
A. That's classic analytic epidemiology.
Q. And you also say in your disclosure together descriptive and analytic epidemiology tools form the foundation by which

epidemiologist explain the distribution and risk factors for disease?

A. That holds true. It doesn't say that it has to always be that way. That's an important distinction.

Q. But both descriptive and analytical epidemiological tools together form the foundation for how epidemiologists explain distribution and risk factors for diseases?

A. Yes.

Q. In fact, as you know from your epidemiologist expertise, descriptive epidemiology, analytic epidemiology, and laboratory components work together hand-in-glove in outbreak descriptions and control. Would you agree with that?

A. Yes.

Q. In fact, I quoted your words.

A. I agree with that.

Q. Can we turn to Tab 27 just to take a look at that document. So, Dr. Klontz, this is a May 19, 2014 e-mail between you and Pamela LeBlanc?

A. Yes.

Q. Who is Ms. LeBlanc?

THE COURT: I don't think he heard you.

THE WITNESS: Was there a question, I'm sorry.

Q. Who is Ms. LeBlanc?

A. Pamela LeBlanc was a member of the CORE team, the Coordinated Outbreak and Response team.

Q. Do you remember this e-mail exchange?
A. Yes.
Q. In the top e-mail you tell her: "That by no means do I want to be obstinate, but as you know from your epidemiology training, descriptive epi, analytic epi, and laboratory components work together hand-in-glove in outbreak descriptions and control."
A. Yes.
Q. Do you agree with that statement?
A. Of course.
Q. Okay.
A. May I comment on that statement? In the OEP we did -- in the Forensic Chemistry we did look at that.
Q. Fair point. We will talk about that more later. You didn't employ any analytic epidemiology in forming your expert opinion, did you?
A. No. No analytical epidemiology other than that, no.
Q. And there's no analytic epidemiology discussed in your disclosure with the document we've been talking about?
A. I didn't conduct any analytic epidemiology in this outbreak.
Q. In your 2015 article there's no analytic epidemiology?
A. It's descriptive epidemiology. That's right.
Q. Now, your -- I want to go back to your disclosure. You give two examples of analytic epidemiology. You mention a

comparison of a group of ill persons against a group of well persons which you call controls. Would you agree with that?
A. Yes.
Q. And a clinical trial where patients given a medical intervention are compared with a control group?
A. Yes.
Q. In both of these examples there's a comparison between the individuals either having an illness or receiving a medical intervention and a control group that does not; correct?
A. Yes.
Q. And, in fact, using a control group is a defining characteristic of analytic epidemiology?
A. In analytic it is.
Q. It's a key feature.
A. Of analytic epidemiology, yes.
Q. Correct. It's the use of a control group that allows the epidemiologist to move from generating a hypothesis to testing that hypothesis; agreed?
A. Testing, correct. Testing, correct. However, may I say that the ultimate tests in this situation was whether the product remains on the market or not. We did a test, if you will. I don't like to think of it that way, but we had enough evidence to say it's most likely OxyElite Pro. We took it off the market. Outbreak went away. It passed the test. That can't be underscored enough here. Was it a classic control

group? No, it wasn't a classic control group, but it was tested. That hypothesis was tested big time.
Q. But the bottom line is no control group.
A. That's correct.
Q. Is that right? Okay. And would you agree that the use of descriptive epidemiology to test those hypothesis, those instances are rare?
A. Explain your question again. What is rare?
Q. Well, rare is what it means --
A. No, just repeat the question.
Q. Epidemiologists can use descriptive epidemiology to generate hypotheses but only rarely tests to hypotheses?
A. With just descriptive epidemiology, that's correct. It's not so much a testing procedure that's incorporated.
Q. Dr. Klontz, you're aware that OEP New Formula was sold in the same formulation in every state of the United States; are you?
A. I was assuming it was very widely sold.
Q. Well, it didn't for New Formulation. Across the country, the same formulation. Would you agree with that?
A. I'm assuming that's the case. I don't have those details. I've been told that it was sold widely in the United States.
Q. Okay. And in your 2015 article you mentioned doing a laboratory component --
A. Correct.

Q. -- section to that.
A. Correct.
Q. The forensic testing for the products that were retrieved from these patients was consistent with the ingredient list on the bottle?
A. That's correct.
Q. Is that your conclusion?
A. Yes.
Q. So is it fair to say that nothing in the OEPNF that was consumed by these patients is any different from the OEPNF that was sold nationwide?
A. Insofar as the sample that our Forensic Chemistry Center tested was representative of the national distribution, I would agree with that. But I don't think it was -- It wasn't a classically random sample obtained from around the country. We have to be very careful on a random sample. I don't believe the FDA did a random sample.
Q. Do you have any evidence to show that the OEPNF that was consumed by Hawaii -- by the patients in your study, I'm sorry, not of just Hawaii -- of the patients in your study was any different than the OEPNF that was consumed by people elsewhere?
A. No, I don't have any evidence to suggest there was any difference.
Q. You're aware that OEPNF was probably sold to millions?

There was a million sales of OEPNF in 2013? Any reason to dispute that number?
A. No, I don't have any reason to dispute that.
Q. And according to your 2015 article and your testimony today, there were 55 cases that had liver disease likely due to the ingestion of OEPNF?
A. Yes. But I would like to say --
Q. Let me ask you questions and will give you a chance.
A. Sure.
Q. And with respect to those 55 cases, at least based on our reading of the patient records that you relied on, 36 of those patients existed in Hawaii?
A. I don't believe 36. I think the case count for MedWatch was more like 27 and there were 22 states that submitted -- of those 55 they reflected illness in 22 different states. Hawaii was number one, California number two, and then --
Q. Do you remember how many -- Let's talk about the MedWatch. Do you remember how many MedWatches came out of Hawaii?
A. My number is I'm thinking it was 23 or something like that. I don't have the exact number. It was the leading state.
Q. But those MedWatch reports, if they were included in the 55, they would have been among the records that you considered forming --
A. Yes.

Q. -- your opinion. Whatever that number is --
A. Yes.
Q. It's --
A. Yes.
Q. Okay. And then you mentioned 22 other states. Do you have any recollection as to the distribution among those 22 states as the rest of MedWatch?
A. It was a national picture. This was a national outbreak. It wasn't a regional outbreak. It was a national outbreak.
Q. Sure, but you've got -- All right. So you've got 21 or 36 patients in Hawaii?
A. Not 36. The low 20s.
Q. What the number is. I will just say -- For the sake of argument, I will adopt your number. 21?
A. I'll say 21 for the sake of argument.
Q. So there's 35 patients left in that 55 patient pool; right?
A. 34.
Q. 34. I'm sorry. I was an English major. 34 patients, 22 states. What was the distribution across -- of those 34 patients across the 22 states?
A. Wide spread from west coast to east coast.
Q. So was it -- What was the highest number of MedWatch reports for a given state among those 22 states?
A. Other than Hawaii?

Q. Yes.
A. California had a good number. 7, 8, 9, 10. Again, I don't have the number.
Q. Of the 55 your testimony is that California -- there was 7, 8, 9, 10 patients from California?
A. California had a handful of cases. Arizona had 3 or 4. There were certain states that had more than one case. The key here is there was a wide geographic distribution of cases by MedWatch, so it was a national outbreak. That's the bottom line.
Q. So if there were 22 states that handed in MedWatches, that means there's -- I'm going to do the math here -- but 28 states that didn't?
A. Now can I get into the perspective on this that I wanted to get to?
Q. Let me finish my question and I will let you --
A. Sure.
Q. All right. So there were 28 states that didn't submit a single MedWatch.
A. Yeah.
Q. Okay. There are 55 patients in your study.
A. Uh-huh.
Q. There are a million sales nationwide.
A. Uh-huh.
Q. Now you can give your perspective. I would like to hear

it.
A. Yes. You need to hear it because in the last year FDA published a paper, peer review paper, indicating that about 2% of dietary supplement-related illnesses seen in emergency rooms, 2% are underreported, highly underreported entity and, in fact, that paper went on to say that looked at a multiplier, 50 -- fair estimates, you need to multiply the amount of reports that come in to these regulatory agencies of dietary supplements by 50. I always see underreporting. It just happens.
Q. But underreporting to the extent of 55 -- 55 out of a million sales?
A. Yes. Yes. That is not surprising at all. That is not surprising at all. Highly underreported in this country. We have a tough challenge to get better reporting. That's one of the reasons I wrote this paper because I believe in MedWatch and I said we've got to do better than this to address just that issue.
Q. Is the purpose of your paper to bolster the MedWatch process?
A. Did my paper bolster the process?
Q. Was the purpose of writing your paper to bolster the MedWatch process?
A. That was not the purpose. Number one, was to get the message out; what happened. Why did this illness happen. How

did it end. How did it manifest before it ended. Number two, was I had a point to make. I had a point to make that we've got a surveillance system at FDA that needs to be used more so we can clarify these relationships between exposures and outcomes. That was a clearly a secondary rationale.

Q. Did you consider -- Going back to control rooms. Did you consider how many people got liver illness during the relevant time frame total, irrespective of OEPNF consumption?

A. In other words, other than -- You are talking about MedWatch reports?

Q. I'm talking about when you wrote your -- When you wrote your report and forming your expert opinion, have you considered the total number of liver injuries from the relevant time period irrespective of OEPNF consumption?

A. I didn't give much thought to that and the reason is because I saw a -- we saw a wave of liver disease of an unexpected number linked to a single product come onto the horizon. I sort of look at -- What you are doing here is I envisioned baseline hepatic disease at sea level. We saw a wave coming at us and that was a wave we couldn't ignore, so I didn't try to measure the depth of the ocean at the baseline. I saw a wave that was a danger to this country.

Q. Dr. Klontz, are you aware that OEPNF went on the market in December of 2012?

A. I read that.

Q. Okay. So how do you explain the outbreak occurring in May 2013?
A. Here is how I explain it. There's an incubation period, number one. Different livers act over different time frames. That's number one. I don't know when the OEPNF got on the store shelves of any state. I just don't have that data. Sometimes I wish I did; that would be even more specific. It could have been a delay in marketing or it could have been a -- a difference in genetic factors of livers that count or some take a longer incubation period than others; among other reasons.
Q. Do you have any evidence to suggest OEPNF has some sort of extended incubation period?
A. I looked at incubation periods pretty carefully and they were generally in the one month to two month range. There were individuals who had taken OEPNF for two years, but I'm assuming DMAA was their initial product and then they transitioned to aegeline and it's hard to calculate an incubation period there if you don't know when they transitioned.
Q. But you have no lab tests or studies to suggest that there's any sort of specific incubation period associated with --
A. I don't have any tests for that.
Q. Going back to the control group. Without a control group

you can't put any mathematical position on the strength of the association you are making between OEPNF and these liver patients?

A. No. There's no mean value you can provide on those, no.

Q. It's a qualitative -- It's a qualitative conclusion?

A. It's a rigorous, qualitative conclusion.

Q. Mr. Runkle asked you about the Bradford Hill factors. Are you familiar with them?

A. Yes, I am.

Q. Do you know -- I'm not testing you but --

A. I know of them, yes. I mentioned some before.

Q. So they would include the temporal relationship between the exposure to and the agent -- exposure to the agent and the harm?

A. Yes.

Q. The strength of the association?

A. Yes.

Q. At this point we don't know because there is no measurable -- this is no quantitative -- no quantitative measurement of that strength; right?

A. Well, association, as strictly defined by epidemiologists, would require a quantitative element to it, but in terms of public health I think that the association -- you could use that word. I wouldn't like to use it but a -- a relationship, a strong relationship between exposure and outcome. That is a

cousin of association.
Q. All right. But strength of association, you are going to -- The best way to understand the strength of association is through some sort of mathematical calculation?
A. Practical. Getting an odds ratio.
Q. Another Bradford Hill factor is dose response relationship; right? In other words, the greater the exposure, the greater the risk of the disease?
A. Yes. And that's true if you've got an idiosyncratic reaction test. The idiosyncratic, not the --
Q. Biological plausibility. Another Bradford Hill factor. Agreed?
A. Yes.
Q. Okay. When we talk about biological plausibility when are saying when an observation is consistent with biological knowledge the observation should be confirmed independently. Is that fair?
A. Yes.
Q. For example, if there was an in vivo study showing an absence of toxicity in mice that would render the association between an agent and a disease biologically implausible?
A. I wouldn't go that far. I would not extrapolate mice to men, necessarily. It could be helpful. It could be -- It could elucidate some relationships there, but the absence in mice I wouldn't say is necessarily safe for humans.

Q. Okay. But it would certainly call into question the biological plausibility?
A. One thing.
Q. And the same with in vitro study in mice?
A. To an extent.
Q. Another Bradford Hill factor. Consideration of alternative explanations; right?
A. Yes.
Q. And then as you mentioned, cessation of exposure. That's another Bradford Hill factor.
A. Repeat that last one.
Q. Cessation of exposure.
A. Yes.
Q. And consistency with other knowledge?
A. Yes.
Q. Do you think I've missed any of the Bradford Hill factors?
A. No.
Q. Now, would you agree that validity of a epidemiologist's finding is a function of his application of the Bradford Hill factors?
A. To some degree. Only to some degree. I think there are situations where, like this one, that you don't need all those factors to take meaningful public action and to operate.
Q. You would at least consider the application of the Bradford Hill factors important from an epidemiological

respect?
A. As I said earlier, an epidemiologist, if he or she is worth his or her dime, always needs to be thinking of Bradford Hill.
Q. Now, in your disclosure don't talk with the Bradford Hill factors, do you?
A. I don't think very much. If I did, I don't think so.
Q. In your 2015 article no discussion of your -- specifically of the Bradford Hill factors?
A. We talked not specifically to Bradford Hill but there's a paragraph in the discussion of sort of the cause effect relationship, and I did use the word "cause" in an epidemiological sense, not a legal one. But, yes, that is essentially a substitute for Bradford Hill, the reasons why we believe that OxyElite Pro was the vehicle of this illness is discussed in that paragraph, a number of factors.
Q. And neither the disclosure nor in the article do you talk about a dose response relationship or do you? I'm not asking --
A. No. Dose response did not have -- No.
Q. No discussion of possible replication of your findings?
A. I'm just trying to think who -- It's kind of hard to replicate an agency's surveillance system. There isn't much -- There are other surveillance systems out there so, no, I didn't dwell on replication. However, I did discuss

rechallenge. I assume we are going to get to the rechallenge. That's not Bradford Hill, but it's a very important observation we made in this outbreak and we may have an opportunity to discuss a 28 year old Hawaiian woman who took OxyElite Pro in March of 2013, became very ill, jaundice, yellow eyes, etcetera, liver function test very high. She stopped taking it; she got better. Her liver enzymes went down. A couple of months later she started again. Boom. They're zoomed up again. That is a very meaningful case. That's a rechallenge. And I know there's an e-mail trail here which you may question me on, but I'm prepared to talk about that. That's a very meaningful case.

Q. I'm not sure I asked you about the rechallenge, so I would like to ask my next question.

A. Please.

Q. There's no discussion of biological plausibility in your disclosure, is there?

A. In the disclosure, no. But the article there is.

Q. Explain the discussion about biological plausibility that's in your article?

A. We referred to the Trilanga study in mice in which a natural constituent did cause liver abnormalities in those animal studies.

Q. Okay.

A. There was some biological plausibility.

Q. So where did you find that article?
A. CDC pointed it out to me.
Q. Okay. Did you do a literature search on the potential hepatoxicity or the effect of the liver on aegeline -- I mean, by -- of aegeline?
A. I did a couple of searches and I found very little in terms of peer review articles.
Q. Okay. Can you turn to tab 34. Okay. Dr. Klontz, this -- We did a literature review of aegeline and we found this handful of studies all of -- most of which -- all of which say that aegeline is not hepatotoxic and many of which say that aegeline actually has some protective properties. Did these come up in your literature search?
A. I'm aware -- I'm aware of some of these articles, yes. I'm aware of some of them.
Q. Okay. And did you consider mentioning them in your discussion on your 2015 article about the biological plausibilities of your proposition?
A. No, I did not.
THE COURT: Counsel, I'm not trying to cut you off. I just want to know how -- how long -- how much more you --
MR. LINEHAN: I've got a fair amount left, Your Honor.
THE COURT: Why don't we take a break then.
MR. LINEHAN: I think that's probably a good idea.

THE COURT: For lunch. We're are at twenty until one and -- How much time do you all want? We've --

MR. LINEHAN: I'm fine with forty-five minutes. I don't want to speak for others.

THE COURT: All right. There are no objections to that. No objections to that, so 45 minutes it is, so -- Let's round it off to -- up to 1:30 then. Just -- Is there something you need to protect in here?

MR. LINEHAN: I mean, we will stay. We will work so --

THE COURT: Okay. That's fine.

(Recess.)

BY MR. LINEHAN:

Q. Welcome back, Dr. Klontz.

A. Thank you, sir.

Q. I want to move to what you actually did in your descriptive epidemiological study. Based on that study, you conclude -- again, I just want to sort of refer back to it -- OEPNF was strongly associated with and most likely responsible for liver decease among the 55 patients described in your article and described in your disclosure?

A. Correct.

Q. In your disclosure you give four bases for that conclusion. Do you recall those bases?

A. In the discussion section you mean?

Q. Well, not with respect to your article. I'm talking about your disclosure. There are four bases that you identify.
A. Okay.
Q. Well, let's turn to that. That's 29. I think it might be 55 at the bottom. It's the second to last page of the disclosure. It's about five lines down. Begins -- There's the word "following." Are you with me?
A. I see -- Page 55; correct?
Q. Yes.
A. Paragraph which starts "Dr. Klontz will discuss" --
Q. Yes. And a little further down it says "first."
A. Yes.
Q. So it says, "Dr. Klontz will discuss the reasons for drawing this conclusion which include the following." Do you see that?
A. Yes.
Q. Okay. And then there are four bases for your opinion.
A. Uh-huh.
Q. Okay. The first one being that the presence of an outbreak of liver disease beginning in May of 2013 was suggested by an abrupt increase in the number of liver cases described in MedWatch reports and medical reports -- medical records received by FDA.
A. Yes.
Q. And second one. "No common factor other than OEPNF

ingestion was identified than could explain the outbreak of liver disease among these patients"?

A. Yes.

Q. Third. "Among the 55 patients with liver disease likely due to OEPNF ingestion, other specific causes of liver disease were symptomatically excluded by treating physicians including a history of excess alcohol ingestion, acetaminophen, presence of viral hepatitis, presence of copper or iron overload, or presence of autoimmune causes of liver disease." Do you agree with that?

A. Yes.

Q. Fourth. "An abrupt increase in reports of liver disease among previously healthy individuals without a history specifically of liver disease strongly suggests exposure among the patients to a common entity responsible for hepatic injury." Those are the four bases of your -- Those are four bases of your expert opinion today?

A. Yes.

Q. And you mentioned a rechallenge patient. Okay? There's no mention of the rechallenge patient in your disclosure, is there?

A. I may not have it. Let me look.

Q. And there's no mention of the rechallenge patient in your article which is incorporated by preference into your disclosure?

A. That's correct.
Q. Okay. Then we've just established that all the bases for your opinion have been stated in your disclosure?
A. Yes.
Q. And those do not include the rechallenge patients?
A. Yes.
Q. I want to go -- I want to go to the -- I want to understand the methodology for the first basis of your opinion which is that -- I want to talk specifically the MedWatch reports. Okay?
A. Uh-huh.
Q. The article and your disclosure talk about 114 adverse event reports FDA received from individuals reporting ingestion of OEPNF. Okay?
A. Yes.
Q. Now, you stated -- Correct me if I'm wrong, you stated that there were these 114 adverse event reports that formed the basis of your conclusion in October 2013 that there was an outbreak related to OEPNF?
A. Specifically, 55 MedWatch reports that were put in a specific group as being called liver disease of unspecified type likely due to OEPNF. Those 55.
Q. But it was the 55 that were drawn from the 114.
A. Yes.
Q. Okay. Now, the fact -- Your article states that the 114

reports were drawn from a period from January 1st, 2011, through February 28th, 2014.
A. Correct.
Q. Okay. So how could that have been the basis for a decision you made in October of 2013?
A. The shape of the curve. When you plot these 55 cases of liver disease that we attributed to OxyElite Pro you see a fairly abrupt appearance of these cases in May of 2013 where as cases before that they just didn't square out.
Q. I understand that. My question is a little simpler, okay? The 114 reports span from January 10th to -- January 10th, 2010, through February 2014; correct?
A. January 2011.
Q. I'm sorry. '11 to February 28th, 2014.
A. Correct.
Q. But you made a decision in October 2013. So how -- How can you make a decision in October 2013 based on MedWatch reports that were pulled from January 2014?
A. A decision -- A regulatory decision was made with the number of cases as of that time.
Q. Okay. So to be clear, the regulatory decision that was made in October 2013 had nothing to do with the 114 reports, MedWatch reports?
A. No. It definitely had something to do with that. Remember, certain subsequent cases by the time the regulatory

decision, remember FDA advocated a recall on November 6th, I believe it was. By that time many of the 55 MedWatch reports, they had already -- they had already had there onset of illness by that time. They were plot-able on that graph. But we extended the surveillance to February 2014 to ensure there wasn't a continuing source of new reports coming on.

Q. Understood. But the decision in October of 2013 can't be based on MedWatch reports that were filed after the fact.

A. Right. That's true.

Q. Okay. So how many MedWatch reports were collected at the point you made the regulatory decision?

A. I would say probably three quarters.

Q. Three quarters.

A. Of the 55.

Q. Of the 55. Okay. What about -- Okay. Now, let's turn to your article. Now, your article talks about -- I'm focusing not on the 55, but I'm focusing on the 114. Okay? Your article identifies 114 reports, adverse event reports, taken from multiple states. Is that right?

A. Correct.

Q. Okay. And you don't remember which states they came from or the distribution among the states?

A. They came from 22 different states with Hawaii being number one in terms of number of reports, California I believe was second, and then Arizona, Minnesota, West Virginia,

Kentucky, Ohio, and on and on.
Q. Okay. Were any of those -- Do those reports come in naturally or did you have any conversations with physicians, you or anyone else with the FDA, have any conversations with physicians seeking out adverse event reports?
A. CDC issued their own -- their own efforts a request for reports of records, so we benefited by those. We came to know about them as a result of CDC's efforts to obtain the cases nationally.
Q. Okay. Who did the CDC make that request to?
A. To the state health departments, primarily, also to a liver disease society, a couple of more select disease groups.
Q. Do you know if the CDC asked all 50 states?
A. Yes. For the state health departments, yes.
Q. Okay. And as a result of that request, the adverse event reports, the 114 is what came in?
A. No, those pre-dated the CDC.
Q. So how many came in in response to the CDC request?
A. Those I don't know exactly how many MedWatch reports came in. I do recall in addition to the MedWatch reports the medical records came in to our office as a result of the CDC reports going forth. So even the CDC requested reporting, it didn't mean it came in the form of MedWatch. Some of these records came to our office in the form of medical records.
Q. Were there any other ways in which these MedWatch reports

were collected?
A. MedWatch constituted about -- of the 114 about 106. There were some other corridors of reporting that were involved, like letters to the agencies, telephone calls to district offices, and so on.
Q. Okay. And were you able -- Of the 114, were you able to identify which ones were filed as in response to a solicitation versus filed during the normal course of --
A. No. I could not ascertain that.
Q. Now, I asked you this morning about -- I asked you before lunch about why there weren't very many reports prior to September/October 2013, given that OEPNF was introduced to the market in December 2014. Do you remember that question?
A. Yes.
Q. Okay. You said that one of the basis for your opinion -- You said that one of the basis for your opinion -- I'm sorry. You said that it was likely due to an extended incubation period?
A. No. If I said that I correct it. I think the lack of reports is most likely due to a passive surveillance being in place. It just doesn't generate a lot of activity.
Q. Okay.
A. Passive surveillance is probably the main answer.
Q. So when did the passive surveillance end?
A. When Hawaii -- September 26, Hawaii media to its

physicians in that state saying we appear to be having a link between dietary supplements used for weight loss and energy enhancement and hepatitis, originally. That's when it -- that's the interpretation.

Q. But before then there were -- Maybe we can look at -- Why don't we look at your curve here, which is on the second -- third page of your article.

MR. RUNKLE: I'm sorry. What tab?

MR. LINEHAN: This is Tab 30.

MR. RUNKLE: Thank you.

BY MR. LINEHAN:

Q. Okay. So explain to me what figure A and what figure B is.

A. Okay. Let's start with actually figure B. Let's go to B first. B is a graph that shows the date of the month for each of the years listed across the lower bar. The date of the month in which FDA received the MedWatch report -- one of 55 MedWatch reports of liver disease.

Q. Okay. What's figure A?

A. Figure A is when you look at each one of those reports the FDA received, what was the date of onset of the illness for each person. So A plots when the people became sick and B is just when FDA received the report.

Q. Okay. Figure A looks like a spike in actual injury occurs in May of 2013; correct? At least begins.

A. I would say May is -- yeah, is consistent with an increased number.
Q. But the spike in reporting occurs, if you will go to B now, spike in reporting occurs in September of 2013.
A. It looks like October, it looks like.
Q. September and October. That's four months later than when the actual injuries were occurring?
A. You are having onsets.
Q. Did you do any analysis or did you look at all into what may have caused the reporting to spike so dramatically in September as opposed to in May when the injuries actually occurred?
A. I attribute it to, as graph A shows, 9-26-13 alert for liver disease for dietary supplements. That was the immediate intervention that I conclude drove the increased number of reports that are reflected in B.
Q. Did you look for any other events in the September time frame that may have caused the spike in reporting in September?
A. I did not find any explanation.
Q. Were you aware of that on September 5th, 2013, a doctor at Queens Medical Center, Dr. Linda Wong, went on the local news in Hawaii and publicly blamed some liver injuries she was seeing on OEP?
A. I vaguely remember. I'm not surprised to hear that.

Q. Okay. Can you turn to Tab 31, please.
A. That date was September 5, you say?
Q. Yeah. Let's just turn to Tab 31. Do you remember seeing -- So this is a September 5th, 2013, article from Honolulu Star Advertiser entitled *Weight Loss Pills May Damage Liver: doctor*. Do you remember seeing this article?
A. I think I've seen that article.
Q. Okay. This article doesn't appear on your figure B, does it?
A. No, it definitely doesn't appear on figure B. Keep in mind, those are both September dates, Dr. Linda Wong and Star Advertiser. September dates. We've still got August, July, a few in May preceding this incident.
Q. I don't have a question, so just wait for the next one. Now, were you aware that -- Were you aware that officials in Hawaii recognized that the media coverage in September may have biased patients reporting on OEP at that time?
A. Where does that conclusion come from?
Q. Let's look at Tab 37. Okay. This is -- This is an e-mail between Dr. Linda Wong, who went to the media on September 5th, and Sarah Park of the Department of Health, the State of Hawaii, talking about having to be called by multiple news people in the Star Advertiser, they want interviews. Do you see that?
A. Uh-huh.

Q. And in the last paragraph she says, "We also got another admitted today from Keiser ... and one is going to be seen at Liver Center on Tuesday. I'm not sure if this is going to increase because there are more cases or because anyone who takes these drugs may be a bit freaked out. The hypochondriacs may start coming out soon." Do you see that?
A. Yes, I see that.
Q. You were not aware of that e-mail or that fact when you put together this epi curve?
MR. RUNKLE: Your Honor, I would object to that question because, obviously, a document that they have never given to us is not a federal government document. Dr. Klontz would not have any ability to --
THE COURT: He hasn't answered yet though.
MR. RUNKLE: I'm objecting to the question.
THE COURT: It's overruled.
A. I'm not aware of it.
Q. Did you ever have any conversations with Dr. Wong about the effect the media was having on reports of OEP in Hawaii in September?
A. None.
Q. Did you ever have any conversations with Ms. Park?
A. The epidemiologist.
Q. Yes. On this particular issue.
A. No, I had no conversations with her.

Q. Did you ever have any conversations with the -- any CDC officials about potential bias reporting in Hawaii?
A. No.
Q. Let's turn to Tab 38. So this is an e-mail from Ms. Park to others -- to Ms. Lauren Lewis and others at the CDC. I want to direct your attention to the second paragraph where it says, "This afternoon the CDC team, Melissa and I, discussed where we are currently, what are the issues and potential options." And in the second paragraph it says, "The team has completed a number of questionnaires but less than 10 compare with greater than 30 reports now. Additionally, it does not appear -- it does appear that the despite our best efforts the public is already biased and mostly by their clinicians in thinking that OEP is the culprit as it's difficult to get them to identify other supplements they may be taking concurrently." Do you see that?
A. Yes.
Q. Did you ever have -- I'm not sure if I asked this question. If I have, I apologize. But have you ever had any conversations with Lauren Lewis or any other people at the CDC about the potential bias that was going on in Hawaii?
A. No, I had no discussions.
Q. Would that have been important in terms of figuring out the significance of the timing of the reporting in September 2013 as reflected on figure B?

A. Let me go back to figure B. That's an attachment. That's like No. 30? What number is that?
Q. Your article?
A. Yes.
Q. 30, I believe.
A. Here we go. Ask the question again. Repeat the question.
Q. The question is: Would a report by the CDC of an observation of bias in the reporting on OEP in the September/October time frame, would that have been significant in your analysis of this epi curve on figure B?
A. I'm not sure how we define bias in terms of reporting, but I stand by the distribution of MedWatch reports of a distinct increase in liver disease in May continuing to June, July, August, all preceding these various dates of media and whatnot. These are individuals who showed elevations of liver function tests, inarguably. They were jaundice. They were ill.
Q. But the -- Dr. Klontz, the spike in reporting happened in September. Is that right?
A. Correct.
Q. Okay. And the CDC report of bias happened in -- around October 1st, in the September/October time frame; right? Relatively the same time period.
A. I'm not sure how they define bias. How do they defy bias? I don't have the answer to that. I don't know what they mean

by that.
Q. A discussion with CDC would have alerted you of this issue?
A. I was in discussion with CDC almost every day. I was in a lot of discussions with CDC. No one ever brought up bias.
Q. In terms of analyzing the timing, the significance of the timing, of the spike of reporting in September 2003, were you aware on October 4th, 2013, a law enforcement called Andrews and Thorton posted a message on its law firm blaming liver injuries on OEP?
A. I don't recall seeing that.
Q. Okay. I want to turn to page -- to Tab 12. This purports to be am October 3rd, 2013 article, posted on Andrews and Thornton's website. Have you ever seen this?
A. No.
Q. Would this have been important in terms of analyzing the significance of a spike in reports in September 2013?
A. It would help explain why there was a spike in reports in September and October.
Q. Are you aware -- Have you ever dealt with anyone at Andrews Thorton?
A. No.
Q. Are you aware they represent many of the passengers that are part of the 55 patient study?
A. I'm not aware of that.

Q. Now, you claim that there was an abrupt increase in the number of adverse event reports in May 2013. We see that on your figure -- on your figure A.
A. Yes.
Q. In assessing the significance of this increase did you do any examination or analysis as to whether there was a spike in acute liver injury generally in the U.S. at that time?
A. No, I did not do that analysis.
Q. How about in Hawaii? Did you do an analysis of whether there was a spike in liver injury in Hawaii at that time, irrespective of cause?
A. No.
Q. Let's talk about MedWatch reports.
MR. LINEHAN: I'm sorry. With the Court's indulgence.
BY MR. LINEHAN:
Q. You are aware with respect to the MedWatch reports that the FDA itself has recognized significant reliability concerns with MedWatch reports. Would you agree with that?
A. I belief that's a reasonable caveat to MedWatch.
Q. Are you aware of what they've actually said about MedWatch reports -- adverse Med reports?
A. I'm not sure we -- I can guess at some things, but I'm not sure what you are referring to specifically.
Q. Okay. Let's turn to Tab 32. So do you recognize this

document, Dr. Klontz?
A. No, I don't. I haven't read this document.
Q. Okay. It purports to be a guidance for the industry that's issued by the Food and Drug Administration on pharmacovigilance practices.
A. Yes.
Q. So are you or are you not familiar with it?
A. I'm not familiar with this document.
Q. Let me direct your attention to page 9. Okay. It's in the discussion on Product-Event Combinations. And a comparison -- It's talking about a comparison of event reports for a given product relative to other products in the same class. It says, "FDA exercised caution when making such comparisons, because voluntary adverse event reporting systems such as AERS or VAERS are subject to a variety of reporting biases. For example, some observations can reflect concomitant treatment, not the product itself, and other factors, including the disease being treated, other comorbidities, or unrecorded confounders may cause the events to be reported."
A. Yes.
Q. Do you see that?
A. Yes.
Q. Is that your understanding of what the FDA's position is on commentary adverse event reporting?

A. It's clearly written there but I have some comments on that, if you will allow me.
Q. So let me go to the next question -- Let me to the next statement. "In addition, AERS or VAERS data may be affected by the submission of incomplete or duplicate reports, underreporting, or reporting stimulated by publicity or litigation." Do you see that?
A. Yeah.
Q. Okay. And is that consistent or inconsistent with your understanding of the FDA's position on adverse event reports?
A. I'm not going to argue with each of those statements. They are reasonable statements.
Q. I would like to show you, just so we have in the record --
A. I would like to say something in that regard.
MR. LINEHAN: Your Honor, I don't think a question is pending.
THE COURT: Okay.
MR. LINEHAN: I would like to, for the record, put in an example of a MedWatch report. Approach?
(Handed to the Court.)
MR. LINEHAN: I'll have the witness authenticate.
THE COURT: Okay. Why are you showing it to me? Did I miss something --
MR. LINEHAN: I didn't show it to you. I was just giving it to you for being marked.

THE CLERK: You don't have your stickers?

MR. LINEHAN: No.

THE COURT: Is this your own copy?

MR. LINEHAN: No, the law firm has 14 copies of everything. I don't know what number we are on but let's just call it Exhibit A.

BY MR. LINEHAN:

Q. So, Dr. Klontz, my question is actually pretty simple. This is an example of a MedWatch report. Would you agree?

A. Yes.

Q. And, in fact, for this, this is the only document we have with respect to one of your 55 patients. I'll proffer that. Does that -- Do you have any reason to believe that with respect to at least some of the patients among the 55 that all we would have is a MedWatch report such as that?

A. Yes. I believe that.

MR. LINEHAN: Do you need this?

(Handed to clerk.)

BY MR. LINEHAN:

Q. Now, you said after receiving patient records from Hawaii you began searching for MedWatch reports identifying OEP consumption. Is that a fair statement?

A. Yes. I asked our data retrievers to pull the MedWatch reports that had been received.

Q. That was from the database within FDA that held the

MedWatch reports?
A. Yes.
Q. But did you do anything more than that in terms of seeking out Med reports? Did you actually actively request?
A. Yes. In certain situations I requested a MedWatch report where we had medical records that were submitted. I requested a MedWatch report.
Q. And that would be the medical records you received from Hawaii.
A. Or some of the states as well. CDC put out a -- what was calling for cases that generated medical records in various states. Those medical records came to my attention for my review and at that point I may or may not have asked for a MedWatch as well.
Q. Okay. And when you asked for the MedWatch reports did the discussion center around OEP?
A. By definition OEP related illnesses.
Q. Did you make any requests, broad requests, for MedWatch reports for liver injuries of unknown etiologies that did not identify OEP?
A. No. I asked for MedWatch reports reflected in the medical records for the case being described in the medical records.
Q. Did you do any survey of liver injury in Hawaii after the recall of OEPNF? Did you do any -- OEPNF. Did you do any analysis or examination of reported liver injury, whether it

was in the form of MedWatch reports or otherwise in Hawaii after the recall of the OEPNF?

A. Only so far as we looked at our MedWatch surveillance system for reports from Hawaii and all other states.

Q. Okay. How long did you do that for?

A. Until the Spring of 2014.

Q. And why did you stop?

A. Because it looked like the cases -- It was one case in January of 2014, one in February, and then March and April were without.

Q. And the February -- The cutoff for the 114 adverse event reports was February 28th, 2014?

A. Correct.

Q. Do you remember seeing or receiving any MedWatch reports after that?

A. I don't remember receiving any beyond that.

Q. Now, I would like to go back to your article just to clarify a couple of minute points. In your discussion about -- In your discussion about the adverse event reports, the paragraph right before the medical reports review, you talk about three adverse event reports that specified death. Do you see that?

A. What page is --

Q. This is page 529.

A. I recall the transplants. I don't recall death. Where

does it say death?
Q. So, in the first paragraph on the second column. The first full paragraph starts: "Three adverse event reports specified death."
A. Okay.
Q. It mentions one in November 2011.
A. Yes.
Q. Years before OEPNF was put on the market; correct?
A. Yes.
Q. That adverse event report didn't report any liver injury.
A. That's correct.
Q. The second death in February 2012. Do you see that?
A. The second death? Yeah.
Q. Okay. February 12 is again months before OEPNF was on the market. Agreed?
A. Yes. No liver disease there, either.
Q. Correct. And then the third death no liver disease there, either?
A. Uh-huh.
Q. Okay. And if you look at your table, in terms of the column that says, and this is on page 530: Liver Disease Likely Due to OxyElite Pro, the middle column. You go down to the last row which says death and the number zero. Is that accurate? I'm sorry. Did you answer the question?
A. I'm recalling the reason I put -- why we put zero there.

These patients were not included in the liver disease -- They did not have liver disease. These patients, none of them had liver disease, so they weren't part of the 55.

Q. So in your studies there was no deaths resulting from liver disease?

A. That's correct. As defined by the 55, there were no deaths.

Q. Your article also talks about the FDA reviewing 21 medical records provided in October 2013 by the Hawaii Department of Health.

A. Uh-huh.

Q. Do you see that? And that's -- That's what we've been talking about, these medical records that they've been sending, that they usually sent you.

A. Yes.

Q. And your article says that this review, quote, "The review revealed that many patients had ingested OxyElite Pro and experienced liver disease in the absence of viral infection, gallbladder disease, autoimmune disease, or other known causes of liver damage. Do you see that?

A. Again, point that out. I am on page No. 1.

Q. So that is in -- If you look at the medical review records section, the first paragraph.

A. Okay.

Q. Do you have any sense of the process that Hawaii

Department of Health undertook when it went about deciding which cases to send to you?
A. They had 27 total medical records we were told which the patients had taken the OxyElite Pro along with another dietary supplement, so 21 reflects at the time, in early October, there were 21 medical records on hand.
Q. Okay.
A. How Hawaii chose those 21, I don't know. They just sent -- That's one reason I was called back. I'm not sure how they picked those 21, but they were OEP patients.
Q. And there were many -- And it says that these records reveal that many patients had ingested OxyElite Pro. Do you know how many is many?
A. Of those 21 I don't have an exact count.
Q. Any reason why you wouldn't put the exact count in the articles?
A. I don't have an answer for you, but I can recall that the majority had ingested OEPNF and that's when I grew concerned and began looking at MedWatch reports.
Q. And how many of these records -- Strike that. So, the article then says that after that review FDA collected medical records from 12 consumers in the continental United States identified from MedWatch reports and reported liver disease after ingesting OEP?
A. Yes.

Q. And are those 12 -- Those 12 consumers, those are within the 55?
A. Yes.
Q. Now, we've taken a look at the 52 files that we have and the state-by-state break down, from our perspective, is that there were 3 from California, 2 from Ohio, and 1 from each of Kentucky, New York, Minnesota, Rhode Island, Virginia, and West Virginia; one in each one of those states. Do you have any reason to think that those numbers are inaccurate?
A. They are not complete. He did mention a few of other states that have cases.
Q. Okay. Which states are those?
A. Arizona is one of them.
Q. Any others?
A. Did you mention Minnesota?
Q. Yes.
A. I know Arizona. After -- I don't have a recollection of filling that in.
Q. Do you have a sense -- Did I miss a lot of states or --
A. Did you mention Florida?
Q. No.
A. Did you mention North Carolina.
Q. No.
A. Those are other states.
Q. So within these 52 patients, files for these 52 patients,

I should have patient files from Florida, Arizona --
A. Arizona.
Q. North Carolina. Any other states?
A. Those are the ones I didn't hear you say.
Q. And as for the rest of the states, there were no reports of liver injury likely due to OEP?
A. Beyond the 22 states.
Q. Again, your article offers no information regarding whether there was a spike in acute liver injury in the continental United States more general, irrespective of cause?
A. No.
Q. Now, let's look at the second page just for your conclusion, which is that no common factor, other than OEP ingestion, was identified that could explain the outbreak of liver disease among these patients. Now, you would agree that in order for this to be a valid basis for your opinion it would have to be true that with respect to the 55 passengers in your study there was a common factor of OEPNF ingestion. As you've mentioned, you reviewed these 55 or 52 files. Now, were you aware that with respect to 12 of these patients there's no mention of OEP consumption anywhere in those medical records?
A. On the MedWatch report there is. Are you talking about MedWatch reports or medical records?
Q. Let's include both in this.

A. By definition, all the MedWatch, all 55 OEP is mentioned.
Q. So for all 55 there should be a MedWatch report?
A. Yes. Yes.
Q. And if that -- And if those MedWatch reports are not included, that would be an incomplete view of what you've reviewed for purposes of your study?
A. MedWatch reports were not included where?
Q. Not included in what we received.
A. There are clearly 55 in this article. There's 55.
Q. Now, you expressed a belief in October 15th, 2013, that when you began reviewing these medical records that the records were a, quote, unquote, "blunt source" for what type of OEP was being ingested?
A. Which records are you referring to? Is this the MedWatch or the medical records?
Q. The medical records?
A. You said "blunt source"?
Q. Blunt source.
A. Where is the word "blunt?"
Q. Okay. Let's turn to Tab 2. Now, this is an e-mail to Roberta Wagner and others?
A. Yes.
Q. You say, "Roberta, regarding patient medical record information on formulations of Oxy Elite Pro that were taken, the data is a bit sparse.

"Usually, the records state that OEP was taken without mention of new vs old. In one record, labels are provided that show the patient took both new (for 2 months) and old (for 7 months). At least one other record noted exposure to the new formulation. I saw no reports indicating the patient had taken, explicitly, on the old formulation. Unfortunately, medical records are a blunt source for new vs old details." Is that accurate?

A. Yeah. Medical records were not very specific in terms of new versus old some of them did, but in general that wasn't the level of detail they got to.

Q. At that point you would go out and talk to the doctors and ask for the MedWatch reports; right?

A. Or already had MedWatch reports.

Q. With respect to certain patients, when you get the medical record, I think you testified earlier that you would ask for MedWatch reports and in response to those requests you get a MedWatch report that mentioned OEPNF.

A. They may not have mentioned NF specifically; it would mention OEP.

Q. But these MedWatch reports would come in after the request.

A. Sometimes. Not always.

Q. And that request -- I think you've testified, that request often made specific mention of OEP?

A. Probably so, because it was the context of an OxyElite Pro

medical record disease.
Q. Did you do anything beyond reviewing the medical records to confirm whether the patients, in fact, consumed OEPNF?
A. No, I relied on medical records and MedWatch.
Q. Let's move to the third basis of your conclusion which is that other specific causes of liver disease were symptomatically excluded by treating physicians including history of excess alcohol ingestion, abuse of acetaminophen, presence of early viral hepatitis, presence of copper or iron overload, or the presence of autoimmune causes of liver disease.
A. Correct.
Q. Although it's not in your disclosure, your article says treating physicians ruled out a role in liver injury not only of viruses but also of autoimmune and all bladder diseases.
A. Correct.
Q. And those -- There's nothing inconsistent with those two statements. Would you agree? You need to do that to diagnose supplement induced liver injury because it's a diagnosis of exclusion?
A. Yes.
Q. In fact, you would agree that the importance of a thorough history in DILI, or Drug and Liver Injury, cannot be overemphasized and that an accurate history of medication exposure at onset and course of liver biochemistry

abnormalities is crucial?
A. The gold standard.
Q. With respect to viral hepatitis, that would include Hepatitis A?
A. Yes.
Q. Hepatitis B?
A. Yes.
Q. Hepatitis C?
A. Yes.
Q. Hepatitis E?
A. Yes.
Q. Herpes simplex virus? Cytomegalovirus or CMV?
A. Yes.
Q. Ebstein-Barr.
A. Uh-huh.
Q. VZV or Varicella Virus?
A. Yep.
Q. Auto-immune Hepatitis?
A. Yes.
Q. Wilson's Disease?
A. Yes.
Q. Okay. Just for clarification, Wilson's Disease is copper overload?
A. Copper overload.
Q. And ruling out all these diseases before diagnosing

supplement induced liver injury is especially critical because a misdiagnosis could keep a physician from treating a disease that's actually causing the liver injury. Would you agree with that?

A. Yes.

Q. Now, on October 31st, 2013, you signed a final health hazard evaluation regarding OEP; correct?

A. Yes.

Q. Let's turn to Tab 6. What is health hazard evaluation?

A. A health hazard evaluation is an internal document that companies every recall of product agency regulates. A health hazard evaluation is just, as its name states, weighs the level hazard deemed to be present.

Q. In this health hazard evaluation -- I'm sorry. With a health hazard evaluation such as this, what would be the regulatory ramifications?

A. Nine months from the health hazard evaluation, it's used in great part to determine the level of recall classification: Classification one, two, or three.

Q. Okay. Did this HHE, did this lead to the recall of OEP?

A. It accompanied the recall of OEP.

Q. Could there have been a recall without this document?

A. At the FDA the two go hand-in-hand. If a recall is deemed necessary or deemed advisable or deemed best for the public health, that is -- that needs to be documented as well.

Q. Okay. So let me go somewhere in this -- on page 3 of 7. You can go down to the last paragraph. Are you with me?
A. Yeah.
Q. Okay. So at this point it looks like there's 27 patients at issue. Is that fair?
A. Yes. That's fair.
Q. With respect to 27 patients they go -- underwent extensive evaluation for no infectious and non-infectious causes of liver disease. Infectious causes that were ruled out after testing include Hepatitis A, B, C, Cytomegalovirus, Ebstein-Barr Virus, Herpes Simplex Virus, Varicella Zoster Virus, and Leptospira?
A. Yes.
Q. What is Leptospira?
A. Bacteria.
Q. It also says that, "Tests also ruled out the following non-infectious causes: Auto-immune hepatitis, Wilson's disease, hemochromatosis, and alpha-1-antitrypsin deficiency." What's hemochromatosis?
A. Iron overload.
Q. And alpha-1-antitrypsin deficiency?
A. It's an enzyme involved in liver metabolism. It can be a damaging health problem.
Q. And alcohol -- Next it says, "Alcohol, liver disease, and/or acetaminophen ingestion were also ruled out"?

A. Yes.
Q. Okay. And it was important for you to exclude these alternative causes of liver because, again, supplemented use liver injury is a diagnosis of exclusion and at this point you were confident enough to put in a memo that these -- that these alternative causes of liver disease were ruled out?
A. Based on the 27 records I had reviewed I had seen enough negative tests among these 27 patients to not be suspicious of any one of these.
Q. So were there tests that ruled out each one of these -- each one of these liver diseases with respect to each of the 27 patients?
A. No, there weren't. There weren't. I did not find a negative test for every patient but I felt there was sufficient negative tests that covered all of these entities different patients but I didn't see a commonality of any one deficiency is a commonality of copper ore or a commonality of iron overload. I was confident that none of these were the problem here.
Q. Okay. But the bottom line is that they weren't all ruled out for each of the 27 patients?
A. That's correct. That's correct.
Q. For each of the diseases that we've mentioned, there are tests that should be run to confirm whether the patient has any of those diseases; right?

A. Yes.
Q. And I know you're not a hepatologist, but you have at least a basic familiarity with the tests that are typically done for these diseases?
A. Yes.
Q. So, for example, for Hep A, there's a Total Hep A and IgM test?
A. Yes.
Q. Are those important tests to run for purposes of excluding Hep A?
A. Yes. IgM is the critical one.
Q. Hep B, there is Anti HBC. By the way, these are all -- just to make clear, these are all antibody tests?
A. Yes.
Q. And done by blood?
A. Yes.
Q. So Hep B there's Anti HBC, IgM, HBsAg, HBV, DNA PCR?
A. Yes.
Q. Any others for Hep B?
A. Some of those will show past immunity but you've covered the ones that show acute infection.
Q. And for Hep C, it Anti HCV and RNA PCR?
A. Yes.
Q. For Hep E, IgM, IGG, PCR. Did I miss any?
A. No.

Q. For Herpes Simplex, IgM -- I'm sorry. Yes, IgM.
A. IgM.
Q. For Cytomegalovirus, IgM, IGG, PCR?
A. Yes.
Q. For Epstein-Barr, early antigen, IgM, PCR?
A. Yes.
Q. For Varicella, IgM, IGG, PCR.
A. Yes.
Q. For Autoimmune, we've got AIH, ANA, ASMA/SMA, F-actin, SLA, LC1/liver cytosol 1. Is that another test that should be run --
A. I'm not familiar with some of the latter ones. Clearly, the former ones that Dr. Bonkovsky spoke of this morning.
Q. What about Total glob AMA?
A. Anti monoclonal antibody.
Q. And LKM?
A. Yes.
Q. Okay. And these are all tests that should be run in order to exclude autoimmune?
A. I don't think they all have to be run to exclude --
Q. At least some of them?
A. Some of them, yes. Can I just say some of these also, you read the literature but not mentioned this morning, can be generated when it's liver disease that's not autoimmune in nature. In fact, some speculate that a supplement that's

damaging the liver can actually for unknown reasons create some of these antibodies.

Q. That's not part of your expert though; right?

A. It's what I've read in the literature.

Q. But your opinion is not based on that. Do you have an opinion on -- I mean, is there an article in mind that you've reviewed for purposes of --

A. Multiple articles. What I'm saying is that the mere presence of one or two of these doesn't make autoimmune hepatitis present.

Q. Okay. And did you consider those articles when you reviewed these patient records to confirm that autoimmune disease was excluded?

MR. RUNKLE: Your Honor, I'm going to object. I've think we've gone pretty far afield from what Dr. Klontz is actually here to testify about, which is epidemiology. We did the liver part of this this morning. He just said that he's not an expert in this, so I don't really -- This isn't a discovery deposition, so I don't really understand what we are doing.

THE COURT: Why don't you testify for me -- I'm looking at your disclosure, expert disclosure. What opinion testimony do you expect from him?

MR. RUNKLE: From Dr. Klontz?

THE COURT: Yes.

MR. RUNKLE: Dr. Klontz is testifying from the epidemiological standpoint that --

THE COURT: Right.

MR. RUNKLE: -- OxyElite Pro New Formula is strongly associated with the outbreak of liver injury.

THE COURT: And that's the extent of the opinion testimony?

MR. RUNKLE: Correct.

MR. LINEHAN: Your Honor, may I respond?

THE COURT: Yes.

MR. LINEHAN: The disclosure and he has confirmed that one of the bases for that opinion is the idea that alternative causes were symptomatically excluded from these patients. There must have been some methodology behind that conclusion and I'm entitled to ask him about that, about the methodology he undertook.

MR. RUNKLE: Your Honor, what I would respond to that is I don't think there's any disagreement between Dr. Klontz and even the defendants about the fact -- how you would look at these facts. This is not a question of methodology. He said that these tests should be done. Obviously, where they are leading is some sort of argument, either here or at trial, that these tests weren't done and Dr. Klontz has already covered that. This is --

THE COURT: He did?

MR. RUNKLE: -- in my opinion -- Yes.

THE COURT: What did he say about that?

MR. RUNKLE: He said that if the tests -- He said that not every test was done for every patient but when he reviewed the tests he believed that there was enough evidence that there was no one common one of those tests that --

THE COURT: Well, how does that square up though with his report that those things were eliminated?

MR. RUNKLE: He said that they were eliminated through -- He said they were eliminated -- and that's part of the problem, why I'm objecting. They were eliminated from the epidemiological sense because they could not have explained all of the injuries. For example, if you -- If there are 55 patients and 45 of them tested negative for Hepatitis B and 10 of them the test wasn't performed, you would exclude the -- you would exclude Hepatitis B as a source of the outbreak. He has already testified about this today.

MR. LINEHAN: I should be allowed -- Your Honor, I may I?

THE COURT: You may go ahead and continue. I will overrule the objection.

BY MR. LINEHAN:

Q. Dr. Klontz, in order to rule out alcohol liver disease one would need to do a toxicology screening; correct?

A. History is important. Potentially a biopsy as well.

Q. And what -- So history of alcohol or a liver biopsy for the purpose of ruling out alcoholic --
A. The history is typically enough and that's routinely done.
Q. And history -- In terms of medical history, how far back would you want to go in terms of -- in terms of establishing whether or not there's a history of alcoholism?
A. A medical history and that routinely goes back a number of years.
Q. Is that true not only for alcohol related -- alcohol related -- alcoholism but in terms of prior potential for liver injury you would want to go back more years and even decades to establish someone, that would be important in analyzing or ruling out other forms of liver disease?
A. Yes. You look at the past medical history of a medical record. That's your opportunity to see if they had preceding liver disease. These people didn't.
THE COURT: Let me ask you a question. Other than the MedWatch records that you relied on, what else forms the basis of your opinion? That's what's not clear to me.
THE WITNESS: 55 MedWatch reports with liver disease. That's one body that I relied on. 55 MedWatch reports. In addition, there were medical records that were separate. MedWatch reports are generated --
THE COURT: I understood that.
THE WITNESS: But the other body were medical

records.

THE COURT: Are those medical records for patients that are included in the 55 MedWatch reports or are they separate? I didn't understand that. I've been trying hard.

THE WITNESS: There's some overlap. We have some MedWatch reports for those patients for whom we also have medical records but we have far more medical records that we don't have MedWatch reports for.

THE COURT: So considering the number of MedWatch reports you have and the number of medical records that you don't have MedWatch reports for, how many individual patients is your opinion based on?

THE WITNESS: 55 MedWatch plus approximately 20 -- 75 patients roughly.

BY MR. LINEHAN:

Q. Are you changing the number of -- Are you changing the number in your opinion from 5 to 75?

A. No. There's -- No. No. There are 55 MedWatch reports. That's a firm number. That's what the article I published is based on. The general knowledge, when you asked where else am I deriving my information from, it's the medical records that I reviewed or which we don't have an MedWatch.

THE COURT: But you are saying there are at least 20 medical records you had which would represent 20 distinct patients from those 55?

THE WITNESS: Correct.

THE COURT: And you reported that previously?

THE WITNESS: Reported it where?

THE COURT: In your report. It's in your --

THE WITNESS: Yes.

THE COURT: It's in your article report.

THE WITNESS: Yes. Talk about in the introduction about how an early October the Food & Drug Administration received 20 medical records from Hawaii

THE COURT: October of --

THE WITNESS: 2013. During the Government shut down.

MR. LINEHAN: Your Honor, may I ask a question?

THE COURT: Yes.

BY MR. LINEHAN:

Q. Your disclosure mentions 55 patients. It doesn't mention an extra 20. Where are these extra 20 patients coming from?

A. Hawaii medical records.

Q. And they are not part of the 55?

A. No, the 55 are the MedWatch reports.

Q. So how many patients are we talking about? Are we talking about 55 patients or are we talking about 75 patients?

A. We are talking about 55 MedWatch plus 27 Hawaii reports that were --

Q. I'm not talking about reports. I'm talking about actual patients. How many patients are there, because we've gotten,

whether it's MedWatch reports or medical records, we've gotten something for only 52 patients. Are you suggesting that there are 20 additional patients that we don't have information for?
A. I assume you -- you can't give medical records on -- the FDA cannot bring its medical records to you. You wouldn't have those, that's confidential --
Q. I will represent to you, sir, that we have medical records as part of this litigation.
A. We wouldn't have submitted those to you.
MR. RUNKLE: Your Honor, there's confusion going on here. It's an obviously specific attempt to confuse this witness.
THE COURT: Well, it's confusing me, too.
MR. RUNKLE: I know --
THE COURT: It's working.
MR. RUNKLE: I know it is confusing you and it is working. There are MedWatch reports and there are patient medical records that Dr. Klontz received. There is some overlap between those two things. His paper which he wrote about is about the 55 MedWatch reports because he is an FDA employee and he wrote about MedWatch reports. These other patient records, which were turned over to the Defense in toto on May 1st, 2017, represent additional patients. They are asking him about that. His original opinion was about 55 patients. They have now opened the door because they are

asking about all these additional things --

THE COURT: My concern, obviously, is what is the basis of his opinion and that's what I can't get a straight answer about, it seems. What is the basis -- You have to have a basis, that's why we are here, of your opinion. What have you reviewed in order to be able to make this statement that you propose to make and I don't understand what the basis is.

MR. RUNKLE: So the basis is MedWatch reports plus the medical records. He obtained a number of medical records and he obtained a number of MedWatch reports. The two emphasize each other. They correlate each other. They corroborate each other. That's what he's saying. And there is some overlap between those two, that some of them --

THE COURT: I didn't hear anything about corroborating it. That sounds like something you said.

MR. RUNKLE: Well, I need to have a chance to redirect this witness.

THE COURT: You will get your opportunity.

MR. LINEHAN: I guess all I want to know is how many patients are we talking about here? Are we talking about 55 patients or are we talking about 76, because all your -- all your disclosure talks about is 55 patients and all your article talks about is 55 patients. Is that the number?

A. It's 55 plus 27 Hawaii medical records, a few of which we have MedWatch reports for, so in the realm of 70, low 70s

number of patients that are the basis for my conclusion.
Q. So there's no reference to those 20 patients in your disclosure. Are you aware of that?
A. Not at this time.
Q. Let's go back to the testing. Actually, let me ask you about the medical records you reviewed. Okay? When did -- when did you start doing them and when did you finish reviewing them?
A. Again, in early October when I was called back here to work and I continued reviewing probably through the end of 2013 into 2014.
Q. Now, did you take notes during that review?
A. Yes.
Q. Okay. Typewritten?
A. Yes. Both written and typewritten.
Q. You have handwritten notes relating to your review of the --
A. Yes.
Q. But you did type them with -- You did do typewritten notes?
A. Yes.
Q. Can you turn to Tab 26, please. So this is a 70 plus page document that was turned over by the Government and they represented this came from your files. Do you recognize this?
A. Yes, I do.

Q. What is this?
A. This is a written summary of the patient-by-patient findings that I extracted from either the medical records or MedWatch or the few here.
Q. There seem to be separate sections of this and I'm hoping you can explain to me how this -- how this -- how your notes are organized here.
A. The initial records are Hawaii cases. You can see Hawaii record numbers. For example, on the first page, there is, on the left-hand column, Hawaii-16, a few lines down. FDA, upon receiving each Hawaii record, generated its own number for clerical purposes, so the first one is Hawaii-16 and 002 would be an FDA number. At the core --
Q. And that's the same as -- That's the same way these things are displayed on each page, there is an I.D. number --
A. Yes.
Q. And there's a Hawaii I.D. number. And it looks like there are columns. Did you create those columns?
A. Yes. Yes.
Q. And there's a column for Lab Results. Do you see that?
A. Yes.
Q. And you would have -- To the extent a lab result, a lab was taken, you would have put that in your notes?
A. That's correct.
Q. And did you have -- Do these notes reflect any separate

discussions you may have had with someone, whether it's the patient or the physician or someone else?
A. No. Strictly from written reports we received, either MedWatch or medical records extracted.
Q. Okay. And if there was a -- Just to make clear, if there was a lab taken it would have gone into your notes?
A. Yes. I may have missed -- I may have not included every lab value in my notes but I looked for high values, in example, in particular, to see how high the bilirubin went, for example. How high the bilirubin went --
Q. Okay. So if we look at the first -- If we look at the first patient record analysis on the first page, is there any notation for any CMV tests?
A. Not on the first page, no.
Q. Any notation for any Epstein-Barr test?
A. No.
Q. Any -- What about Varicella?
A. No.
Q. Hep B?
A. No.
Q. Herpes Simplex?
A. No.
Q. Any reference to a toxicology screen?
A. No, but that's also in the history -- not just lab tests but alcoholism it would be in the history.

Q. Any mention of an acetaminophen test?
A. It might be in the history as well.
Q. Let's go to the next one. This is patient No. 3.
A. Yes.
Q. Any reference to a CMV test?
A. No.
Q. Any reference to an ABB test or Epstein-Barr?
A. No.
Q. Varicella?
A. No.
Q. Hep B?
A. Acute, yes. Acute Hepatitis Panel A. That would include A, B, C, B.
Q. So when there's a Hep panel, a reference to a hep panel would have been across the board?
A. Yes.
Q. Herpes Simplex?
A. No.
Q. Any reference to a toxicology screen?
A. No.
Q. Acetaminophen?
A. No.
Q. Let's go to the next one. This one we have mentions of DBV, VZV, HSV, Hep E, Hep A. Hep -- Hep B, Hep C, autoimmune. Was there autoimmune mentioned in this one? Yes, there is.

A. Yes. And kidney.
Q. Let's go to the next one.
A. Which number are you on now?
Q. I'm on -- This is VA-1 HI-38. And you mention herpes simplex?
A. No.
Q. Hep B?
A. Hep E did you say?
Q. Hep B.
A. Hep B. Nope.
Q. Okay. Let's go to No. 5. Any mention of Hep C?
A. No.
Q. CMV?
A. No.
Q. Epstein-Barr?
A. No.
Q. Varicella?
A. No.
Q. Herpes Simplex?
A. No.
Q. Hep E?
A. No.
Q. Autoimmune?
A. No.
Q. Ceruloplasmin?

A. No.
Q. The next one. Number 6. Any mention of CMV testing?
A. No.
Q. EBV or Epstein-Barr?
A. No.
Q. Varicella?
A. No.
Q. Herpes Simplex?
A. No.
Q. Hep B?
A. No.
Q. Hep C?
A. No.
Q. Any mention of a tox screen or an acetaminophen test?
A. Test in the history, yes.
Q. Patient 7. Epstein-Barr. Any mention of Epstein-Barr testing?
A. No.
Q. Varicella?
A. No. I don't see it.
Q. Herpes Simplex?
A. No.
Q. Hep B?
A. No.
Q. Mention of a tox screening?

A. Nope.
Q. Any mention of an acetaminophen testing?
A. No.
Q. Ceruloplasmin?
A. No.
Q. Let's go to 9. Any mention of a -- of Varicella?
A. Nope.
Q. Any mention of a tox screen?
A. No.
Q. Okay. And we've got Hep B. That's pending at this point; right?
A. We've got Hep E, IgM core HB is negative.
Q. That's Hep B or E?
A. Hep E.
Q. Hep E is pending.
A. Yes.
Q. So no results there. Let's go to 10. Any mention of Herpes Simplex?
A. No.
Q. The tox screen?
A. No.
Q. Okay. 11 is fine. Let's go to Hawaii 11. Do you see that?
A. Yes.
Q. Any mention of Varicella?

A. No.
Q. The tox screen?
A. No.
Q. Okay. Respect to Hawaii-10. No mention of CMV. No mention of Epstein-Barr. No mention of Varicella, Hep B, Herpes Simplex, toxicology screen, or acetaminophen?
A. No.
Q. Did you ever, based on your notes or based on the medical records, did you ever look for any patterns in how many patients were tested for what in terms of -- in terms of verifying the data in an aggregate way?
A. I worked for the CDC at CDC's request to record liver enzymes and code ability of them and where the data existed or various tests you are asking about. CDC did collaborate on that.
Q. Do you have any notes regarding how many of these 55 patients took test A versus test B versus test C? Do you have that in the aggregate form?
A. No, just what we see here and in addition CDC in their study, there's 7 cases that met their case definition.
Q. So we've done that aggregation based on a review of the medical records. Were you aware that 28 of that 55, 52 patients whose files with we have, according to their medical records, were not tested for CMV?
A. I don't dispute it.

Q. Were you aware that 29 were not tested for Epstein-Barr; 46 were not tested for Varicella; 39 were not tested for Herpes Simplex; 46 were not tested for Hep E; and 18 were not tested for Wilson's disease?
A. Okay.
Q. Does that surprise you?
A. No, it doesn't surprise me. These tests -- to have every one of these test conducted on every one patient I don't think it would happen very rarely, very rarely, and what I'm reassured is by the following: Is that if any one of those things had been the cause of the outbreak you would have seen continued transmission. Those things would have continued happening. There would have been disease -- OxyElite Pro off the market wouldn't have affected the outbreak if it was due to any one of those.
Q. But you haven't done that examination, have you?
A. To my knowledge, there's no reports of ongoing epidemics of Herpes Simplex virus, hepatitis, VZV hepatitis. Hepatitis E virus. We've got a very good infectious disease surveillance system in this country. We are not seeing ongoing transmission of those.
Q. But any one of these is patients could have a different form of virus and it wouldn't be an outbreak.
A. It's possible, but it would be an exceedingly large number.

Q. We don't have a basis -- We don't have a comparison against the general number of liver diseases in Hawaii or nationwide because you haven't looked at that?
A. That's true but you would still have an exceeding number to explain this outbreak on any of these entities you mentioned that weren't tested for. It's a very rare phenomena. If it happened in the continental United States and Hawaii it would be very unusual.
Q. So the 22 cases in the continental United States and the 36 cases that are in Hawaii --
A. Over a 2,000 mile expanse of land.
Q. Out of a million sales of OEPNF in 2013?
A. If you're asking me as a epidemiologist, I find that exceedingly unusual. I was confident, after reviewing this data, notwithstanding the gaps in laboratory test, that we had found the culprit.
Q. But you do agree that in order to diagnose for supplement induced liver disease you need to exclude all the diseases we are talking about?
A. I do. I do. That's the gold standard.
Q. Okay. That's the gold standard. Now, back in 2013 you reached a conclusion similar to the opinion you are offering today that based -- at least on some of the patients among the 55 at that point there was an outbreak in Hawaii based on OEP?
A. Yes. Not just one.

Q. And do you remember -- Do you remember a call, a conference call that you participated in with respect to representatives from USPLabs?
A. Yes, I do remember that.
Q. Do you remember any e-mail exchange that you had?
A. Yes.
Q. Let's go to that. Tab 9. So this is an October 4, 2013, e-mail exchange with you and others. What -- What organization are these other individuals from?
A. All FDA.
Q. Okay. This was in preparation for a call you were going to have with USPLabs in mid October?
A. Yes.
Q. I want to talk a couple of these e-mails, but I would like to turn you to the e-mail from -- that you send with the time stamp 9:24 a.m. It's on the second to the last page of this exchange.
A. Yeah. Okay.
Q. Okay. So the second paragraph you say, "I also want to steer clear of wading into highly-detailed results of findings such as those from individual liver biopsies or whether, say, serologic markers do or do not provide sufficient reason to diagnose an underlying auto-immune condition of the liver. These sorts of discussions are best had between their hepatologist and a counterpart from FDA. Because I am not a

hepatologist, I am not well-versed in the nuances of liver pathology." Do you see that?

A. Yes.

Q. In your next paragraph you say, "But as an epidemiologist I recognize an outbreak when one occurs." Was that a scientific methodology?

A. It's based upon the review I had done until that time based on medical records and MedWatches.

Q. So the same medical analysis that you are trying to avoid in your prior e-mail?

A. Trying to avoid?

Q. You don't want to talk to the hepatologist, you want to do clinical --

A. I would like to comment on that. The reason I suggested FDA is that we hold off on conversations with the company was because I was concerned if they had a liver specialist I wouldn't be the agency's best representative to carry on those discussions. I do say if it's going to be epidemiologic matters I'm fine being on that call. But if the goal is to talk about nuances of liver cells, be abnormal here or there, I'm not the person to do it. That's why I mentioned that. I wanted to see a level playing field in terms of liver pathology, a discussion with that direction.

Q. Okay. So in a later e-mail it wasn't just you, you wanted the group to avoid that discussion?

A. I wanted to have the proper people on the call. That was my main concern.
Q. Did that call ever happen?
A. I don't recall that call happening. I don't recall it.
Q. Did -- Was there a hepatologist involved at the FDA in real time?
A. I don't think we ever recruited a hepatologist from the Center for Drugs. We didn't get that far.
Q. Did you ask?
A. No, I don't think it was deemed necessary, given that there wasn't a call lined up.
Q. Now, we talked a little bit about medical history and the importance of medical records that date back I think you said even back as far back as decades.
A. In the past medical history part of a medical record, yes.
Q. And one of your base -- another bases for your conclusion for your expert opinion here is that the medical records, is that the patients, the 55 patients were previously healthy individuals without a history specifically of liver disease?
A. Correct.
Q. And in order to determine that you would need to go back, as you say, decades. Am I right?
A. You would ask in your history -- Physicians taking a history would ask have you ever had hepatitis, have you ever had liver disease, yes.

Q. Did you confirm that the medical records reflected that that discussion occurred?
A. If there was no mention of past medical history of previous liver disease I assumed there was no history of previous liver disease.
Q. Records that would complete that medical record would have shown that notwithstanding the absence of any notes in the medical record you had access to?
A. I'm not sure what you are asking.
Q. Let me ask it another way. When we look at these records with all -- all with respect -- all with the exception of 5 don't go back further than 2013. Would that be more or less consistent with your recollection of the dating of the records that you reviewed?
A. The actual medical records when they are recorded may have dates that don't go back before 2013, whatever you said. But in asking patients the questions, they go back in time well before 2013.
Q. So if there's no report that that discussion occurred in the 2013 records, we don't know what happened prior to '13 without records pre-dating --
A. No, that's not right. A physician would ask about preceding life medical events in 2013 when examining and taking a history.
Q. I understand. I think you misunderstood my question.

What I'm saying is if the 2013 medical records don't reflect that that discussion ever took place then the only way that you can confirm that these patients were previously healthy would be to see their complete medical history?

A. Yes. And if the past medical history made no mention of it by training physicians would assume there was no previous disease.

Q. So --

A. That's standard past medical history.

Q. So with respect to your review of taking the medical records, you never said, hey, let's follow up, let's get some older records, I want to confirm that these guys -- many of these guys were previously health?

A. No.

Q. What about time to onset of illness. Do you think it's relevant? Do you think the fact of the time between the patient's stopping the consumption of the product and the onset of illness, do you think that's an important factor to consider in whether or not OEPNF was the cause of the liver injury?

A. More importantly, the question is when did they start taking it and the onset occurred. Are you asking now for those that stopped taking it and then it developed?

Q. Correct.

A. That was very uncommon. Most individuals started taking

it, continued taking it, and developed liver disease. There were a few, there were a few, that stopped with subsequent onset of illness suggesting to me that the damage had occurred when they stopped and didn't matter until X number of --

Q. Now, we talked about biological plausibility as one of the Bradford Hill factors and part of analyzing biological plausibility is figuring out whether the substance in question has any proof that as a biological matter causes the injury that we're looking at; right?

A. Uh-huh.

Q. Okay. And you talked about aegeline and you talked about the 8195 article, etc. Did you -- and I think -- I think what you testified to this morning was that maybe it's not conclusive but at least it's relevant the existence of in vivo testing or in vitro testing that may or may not show hepatotoxicity. Is that fair?

A. It shows there is toxicity. That's relevant.

Q. Okay. Would it not be relevant if it didn't show toxicity?

A. I would have to see the study and the extent of studies do that. I would be more cautious about the lack of evidence than any presence of it.

Q. So if a test concludes that it's hepatotoxic you only need one and if it shows that it's not hepatotoxic it sounds like you need multiple --

A. I would steer in that general philosophy, yes. That would be my style, yes.
Q. Now, you were here when Mr. Bonkovsky was asked about a study that was conducted by the FDA in vivo and in vitro --
A. I was here.
Q. Were you familiar with that testimony you heard about?
A. No.
Q. Did you know -- Do you know Thomas Flynn?
A. No.
Q. Do you know Yitong Liu?
A. No.
Q. Martina Ferguson?
A. Martina Ferguson? Statistician. I know who she is, yes.
Q. What about Sheila Pugh Bishop?
A. No.
Q. Those are the authors of it. But you do know Martina Ferguson?
A. I know who she is.
Q. But you haven't talked to her?
A. No.
Q. Just -- I'm sorry. You were not aware that that -- that test was taking place?
A. Generally, I heard that there was some animal tests. I knew nothing about protocols.
Q. What exactly did you heard?

A. There was animal testing.
Q. On OEP?
A. Yes.
Q. Did you hear there was testing on OEPNF and the ingredients as well?
A. I have no --
Q. Did you ever follow up on what the results of those tests were?
A. No.
Q. Let's go to Tab 19. So this is the test that my colleague talked to Dr. Bonkovsky about this morning. If you can turn to page 15. The same page we talked to Dr. Bonkovsky about. So the second paragraph starts, it says, "The overall conclusion from the present studies is that they failed to provide a 'smoking gun' that would definitively identify OxyElite Pro of any of its components as a frank liver toxicant." Do you see that?
A. Yes.
Q. Would that have been important to you know at the time you formulate it your opinion?
A. No. And I'll tell you why. In previous dietary supplement outbreaks I've been involved in, investigating, such as I mentioned, Eosinophilia-myalgia syndrome, now tryptophan, mechanism, speculative, but not really certain; Hydroxycut, speculative but not certain. These are just -- A

lot of these things can be very mysterious, complex things. I'm not surprised by the statement, to answer your question.

Q. Were you aware of a test that was done -- the other test that we talked about with Dr. Bonkovsky, were you aware of the test done by Dr. Khan?

THE COURT: Counsel you are starting to sound a whole bunch like cross-examination based on facts.

MR. LINEHAN: Okay. Well I -- I would like to explore his methodology in terms of whether he examined -- sufficiently examined the plausible -- the biological plausibility of other causes which is a factor in the Bradford Hill battery of factors.

THE COURT: That's not what you are asking him. You are asking him what he thinks about other people's opinions.

MR. LINEHAN: If I -- If I was asking him about his opinion on others, I'm just trying to establish what he reviewed in terms of a biological plausibility.

THE COURT: Did you review something other than MedWatch report and the 20 or so medical records?

THE WITNESS: That was the body of --

BY MR. LINEHAN:

Q. And you were not aware what of those tests?

A. Which tests?

Q. The two test that we're discussed with Dr. Bonkovsky this morning.

A. No. I'm not familiar with them at all.
Q. The opinion expressed in your disclosure is that OEPNF was strongly associated with and most likely responsible for the liver disease among 55 patients.
A. Yes.
Q. You article -- Your article actually says something a little different, okay? It says, "Findings from case series such as this one cannot be used to draw definitive conclusions about the role of OxyElite Pro as the cause of liver injury." Do you remember that?
A. Yes. I don't see an important difference between those two.
Q. Okay. Well, then you say, "Several observations support the plausibility of a causal role."
A. Yes.
Q. So that's the opinion and that -- that article was peer reviewed; right?
A. Yes.
Q. Okay. And that's the opinion that was peer reviewed?
A. Uh-huh.
Q. Not the opinion that you are offering today in this disclosure.
A. From an epidemiologic standpoint there's not a whole of difference when it comes to public health. There's not much difference between any of those statements when it comes to

public health. We had a product --

MR. WEINGARTEN: Your Honor, can I just object? I've been trying to be very patient. He loves to editorialize and he gets the -- The questions -- They are asking him a question, he gets an answer, but then he wants to go on and this is another illustration of exactly why with we are here still here at this hour. I'm objecting to him not answering the question. His responsiveness is not correct.

MR. RUNKLE: Your Honor, I would object to the cross-examination nature of where this has gone. They are not entitled to a discovery deposition of my expert witness and I think we've gone very far afield at this point.

MR. LINEHAN: Your Honor, if I may -- If I may press with these couple of questions whether -- whether a study has been peer reviewed a clear factor under *Daubert*.

THE COURT: Agreed.

MR. LINEHAN: And if his disclosure opinion wasn't peer reviewed then I think that's relevant to his overall analysis.

THE COURT: Okay.

BY MR. LINEHAN:

Q. So, Dr. Klontz, are you suggesting that plausibility is the same thing as strong association and most likely responsible for?

A. Repeat the question, please.

Q. So in your -- In the peer reviewed article you say there is a plausibility of a causal role of OEPNF?
A. Yes.
Q. Yet, in your disclosure you say it's strongly associated with and most likely responsible for. Is it your testimony that those two things are the same thing?
A. From a epidemiologic public health standpoint, I wouldn't parse those a whole lot. It wouldn't make much of a difference between them. May I embellish?

THE COURT: When the prosecutor stands up, if he wants you to continue, you may do so.

BY MR. LINEHAN:

Q. Just two more questions. You are here as an expert in this case to look objectively at whether or not OEPNF was strongly associated with liver injury or essentially what you are doing is you are reviewing your own work back in 2013; correct?
A. Yes.

MR. LINEHAN: No further questions.

THE COURT: Any other Defense counsel?

MR. MCMULLEN: Your Honor, there's something I would like to clarify.

THE COURT: Come on up. For the record, please state your name again.

MR. MCMULLEN: Yes, Your Honor.

CROSS-EXAMINATION

BY MR. MCMULLEN:

Q. Good afternoon, Dr. Klontz. May name is Joseph McMullen and I represent SK Labs. I was sitting way in the back there and so I might have misheard this, but when you were discussing how you arrived at your opinion this afternoon, I understood you to say that there were 27 total medical records you received from Hawaii in which the patients consumed OEP along with another dietary substance. Did I hear that correctly?

A. Incorrectly. There were 27 medical records from Hawaii in which the patients ingested OEP and potentially one or more other dietary supplements. I'm sorry. The 27 were just OEP plus or minus others, but they each had OEP ingestion.

Q. Did you determine what those potential other dietary supplements, one or more, were?

A. If they were listed in the medical records, yes, it was apparent and there were no commonalities other than OEP. In other words, there was no alternative explanation of other dietary supplements beyond OEP.

Q. Did you review what the underlying active ingredients were in those other dietary supplements?

A. Yes. Yes. For example, I -- yes, I -- I do recall looking at that, yes.

Q. And you determined whether there were commonalities in the

underlying active ingredients in these other dietary supplements?
A. Commonalities. What do you mean? How do you define that?
Q. The same active ingredient in other dietary supplements that were being taken amongst these 27 patients?
A. I didn't do as -- perhaps later -- I did look and see the general nature of those other supplements that were -- side-by-side, no.
Q. Were there some that were in common?
A. There were one or two other dietary supplements that were mentioned, but that's it.
Q. Beyond dietary supplements, in your methodology did you determine whether there were other non-dietary supplements substances that were being ingested in common amongst the other -- these 27 medical records?
A. Medications for sure. I looked at the medications in the medical record to see what they were taking in terms of prescription drugs.
Q. Did you determine if there were other substances in common amongst them?
A. I did not find any.
Q. Beyond medications did you determine whether there were other substances in common amongst these 27 medical patients?
A. I am relying on the medical record and I saw no other commonalities mentioned.

Q. Okay. Was it important to your methodology in arriving at your opinion regarding an alleged association between OEP and liver injuries to know whether there were, in fact, other substances in common amongst the 27 patients?

A. That was a key -- that was a key interest of mine to see if there were other commonalities beyond OEP, yes.

Q. Did you do any follow-up with those 27 paints to make sure that there was robust questioning as to what substances in common they may be taking?

A. No. I took the word of the medical records and made the assumption that the physicians who were diagnosing and treating these patients did that.

Q. And these were records coming from Hawaii?

A. Yes.

Q. And records where there, as you are aware, potentially issues as to media bias; correct?

A. They are records from Hawaii, physicians, and that's it.

MR. MCMULLEN: I don't have any further, Your Honor. Thank you, Dr. Klontz.

THE COURT: In this other Defense counsel? Redirect.

REDIRECT EXAMINATION

BY MR. RUNKLE:

Q. Dr. Klontz, thanks for sticking around here this afternoon. I know it's been a while. So if we could turn to in your binder here, let's turn to your paper, which I believe

is Tab 13. If you could turn to page what I believe is page 529. You discuss a medical records review that you conducted. Is that correct?

A. Yes.

Q. And those medical records are not the same as the MedWatch reports that you discussed earlier on your paper. Is that right?

A. Yes.

Q. Right. So you did disclose in your -- You disclose exactly what you reviewed in this document. Is that right?

A. Yes.

Q. And you gave those medical records to me on a thumb drive a year ago. Is that right?

A. Yes.

MR. RUNKLE: Your Honor, I would offer the Court that those medical records were turned over and those are in addition to the MedWatch reports and it is adequately described in his disclosure. All of what he is relying on is described in his disclosure.

BY MR. RUNKLE:

Q. So, do you think Mr. Linehan understands your paper?

MR. LINEHAN: Objection?

BY MR. RUNKLE:

Q. Let's move to Tab No. 6. Now, Mr. Linehan asked you about the onset of this outbreak; right? Do you remember that?

A. Yes.
Q. And you said that the onset of this outbreak was in May 2013. Is that right?
A. Yes.
Q. If you can look at this paragraph right here, and Mr. Linehan forgot to talk about this, there is a sentence in here that says, "USPLabs ceased distribution of the DMAA-containing versions of OxyElite Pro in May 2013 and destroyed all remaining stocks held by the company." Does that refresh your memory about what was going on in May 2013?
A. Yes. Yes, it does.
Q. As an epidemiologist, what does that tell you about the onset of the outbreak?
A. It suggests to me that DMAA is no longer available and as people become ill it most likely reflects the ingestion of the New Formula --
Q. Right. So the fact that product was on the market in November 2012 is not as -- is not as strong of evidence of the fact that their other product was off the market in May 2013. Is that right?
A. Yes.
Q. Now, Mr. Linehan asked -- he spent a long time asking about a number of tests that may or may not have been performed on these -- on these patients. So if we could turn to Tab 26. Is every test that was performed on every patient

in this document?
A. Not every one, no.
Q. Did you endeavor to put every test that was performed on every patient in this document?
A. As I mentioned, some lab values I just didn't put on but I attempted to capture those that represented the major categories.
Q. And so one of the things that Mr. Linehan asked you often about with CMV. What's that?
A. Cytomegalovirus. It can cause a hepatitis picture.
Q. Have you ever seen an outbreak of acute hepatitis like this caused by CMV?
A. No, I have not.
Q. How many outbreaks have you studied?
A. Outbreaks in general? Hundreds.
Q. Does CMV cause these types of liver injuries?
A. I want -- I haven't seen a CMV hepatitis outbreak, so I can't tell you that.
Q. What's Epstein-Barr?
A. Epstein-Barr is a DNA virus.
Q. Have you ever tracked an Epstein-Barr hepatitis outbreak?
A. No.
Q. You've never seen injuries like this called caused by Epstein-Barr?
A. No.

Q. What is Varicella?
A. Varicella? It can remain latent. Causes shingles, I think.
Q. Have you ever tracked a Varicella outbreak of liver injury like this?
A. No.
Q. You've never seen that in your career?
A. No.
Q. What about herpes?
A. The same answer. I haven't seen it.
Q. Never seen anything like that?
A. No.
Q. How about Hepatitis E?
A. I have not seen Hepatitis E outbreaks in the United States. Read about them in Africa, but not here.
Q. In your experience as a hepatologist which now tracks more than 30 years, you have never seen any type of outbreak that -- none of these causes could explain the outbreak that you saw here. Is that correct?
A. You said "hepatologist." Epidemiology.
Q. I'm sorry. In your years of epidemiology. Excuse me. In your years of epidemiology have you ever seen an outbreak caused by any of those causes that looked anything like this?
A. No.
Q. Have you ever seen any reports in the literature of

outbreaks that looked like this that were caused by any of those causes?

A. No, I have not.

Q. There was also questioning about Hepatitis B and antibodies; right? And so some of these tests, they can be positive tests for antibodies but they don't reflect an acute illness. Is that right?

A. Yes.

Q. Sometimes there could be a positive hepatitis test and it doesn't reflect an acute illness. Is that right?

A. It reflects a past infection.

Q. Past infection.

A. Long ago.

Q. So there's another commonality in some of these patients that I would like to talk about which is their race. Was there any commonality that you saw in the race of these patients?

A. There was a higher preference of proportion of patients with Asian -- mixed Asian dissent, yes. I -- This is a fact that caught my interest. Yes, there was.

Q. And have you seen other outbreaks that -- of injuries that target a very small part of the population like that?

A. In terms of what kind of outbreak?

Q. In terms of a food borne or a dietary supplement borne outbreak?

A. No, generally it's not racialized.
Q. So that was very unusual, in your opinion?
A. Yes.
Q. And in your experience as epidemiologist you took that into account?
A. Yes.
Q. Now, there was a lot of other discussion about whether you perform analytic epidemiology.
A. Yes.
Q. How long would that have taken?
A. To do a case control study would have been substantial time. Two to three weeks probably, at least.
Q. And during those two to three weeks possibly more people would have fallen ill?
A. Absolutely.
Q. So you think you made the right call at the time; right?
A. I have no doubt about it.
Q. You have no doubt about the fact that OxyElite Pro was associated with this outbreak?
A. I have no doubt about it.
Q. And your 30 years of experience. Is that right?
A. Yes.

MR. RUNKLE: Thank you, Your Honor.

THE COURT: Any recross? Limited to what?

MR. LINEHAN: It's going to be five questions.

RECROSS EXAMINATION

BY MR. LINEHAN:

Q. Dr. Klontz, Mr. Runkle asked you about consideration of whether or not there was something with respect to the patient's race that may have contributed or may explain the association that you --

A. Yes.

Q. Did you explore that at all?

A. I had a number of discussions with CDC about it, yes.

Q. You mentioned never having talked to Thomas Flynn?

A. I never talked to him.

Q. You never talked to him about the possibility of testing for race in the context of OEP?

A. I did to an -- an epidemiologist, but I do not recall --

THE COURT: When you were talking about the race of the patients, were you talking about the 21 medical records --

THE WITNESS: In general. The outbreak as a whole.

THE COURT: The outbreak as a whole.

BY MR. LINEHAN:

Q. Can you -- Can you turn to tab 36. Okay. So this is a -- This is proposal done by Thomas Flynn and Yitong Liu, the same researchers who did the OEP study that we talked about during my direct examination and he is proposing to incorporate ethnic diversity into in vitro hepatotoxicity testing. Does that refresh your recollection as to the possibility you may

have discussed this with Thomas Flynn?
A. I can't remember at all. I don't recall discussing this with Thomas Flynn.
Q. If you would go to the second paragraph. It refers to native Hawaiians and Pacific Islanders exhibiting the highest rate. And then there's a reference in the second -- the third sentence says, "Limited medical information on twelve of the OEP cases showed that one had normal weight, three were overweight, and the remaining eight were obese," and then he attributes that to a personal communication from you?
A. I don't recall it.
Q. Mr. Runkle also asked you about -- asked you about the speed with which you needed to identify the outbreak.
A. Yes.
Q. Was there ever any attempt to do a case control study after OEP was recalled?
A. No. No, there wasn't. The problem with that, if I may answer this, is that there's been post facto, if you do case controls after the fact, there could be all sorts of problems in terms of the bias there.
Q. So bias was an important consideration in that decision --
A. Well after -- After we made our decision, there was no discussion of the case.

MR. LINEHAN: No further questions, Your Honor.

THE COURT: Any other Defense counsel on recross?

You may step down, sir. I think before I hear additional arguments that are related to the two doctors who testified here today before we go onto a different motion.

MR. RUNKLE: I always have argument but I don't know if it's necessary. From what we filed and what we presented today.

MR. NIEWOEHNER: Your Honor, I will speak on Dr. Bonkovsky for a minute.

Your Honor, for Dr. Bonkovsky, there are two categories of statements from him. The first one is his statements about his perception that there's no benefit to OEPNF. He said things like it should never have been sold. Essentially, Dr. Bonkovsky has the opinion that if there is no clinical trial, then there is no benefit. It's a dietary supplement, at the very least. That's clearly his subjective belief and under *Daubert* reasoning it is not grounded in either the law, practice, or research. He is just off on his own with his own personal view of this. But he could not -- he could not identify a grounding for himself in assessing the benefits of dietary supplements. So we would seek to exclude that aspect of any opinion he made.

THE COURT: It seemed to me they were attempting to clarify and actually did say in the -- although he misspoke here initially his opinion wasn't that there was no benefit but that there was no evidence of any benefit. So does your

objection go to that? That's why I asked him that, because he said -- what you said at first I believe, but the disclosure actually said something else and so when I asked him again he seemed to come back to the proposed opinion that was in the disclosure which kind of gave --

MR. NIEWOEHNER: Even I guess that lesser statement --

THE COURT: Because it's really not an opinion as much as a fact, I guess.

MR. NIEWOEHNER: Except he didn't do what you need to do, he didn't do any research to establish that.

THE COURT: Research to establish research?

MR. NIEWOEHNER: Yes. He didn't check for articles that -- sort of basic step to determine whether there is any evidence, you go look for it. He didn't do that. He wasn't asked to do it. So he is just opining today based on, quite frankly, a view of the dietary supplement industry. That's fine. He is entitled to his opinion. But it should not be introduced into this case as expert opinion.

With respect to his other statements about the harm caused by that. I do want to flag a couple of things that -- You obviously read our briefs. I'm not going to -- I'm going to try not to repeat anything. But one thing I do want to highlight is the prejudice that is a prong of the *Daubert* analysis Rule 403. What Dr. Bonkovsky's testimony is relevant

to is really only one count in this indictment, Count 10, a misdemeanor count, that accuses the Defense of essentially distributing a dietary supplement that poses a risk of injury. As a result of that misdemeanor count, I fully anticipate that they will be seeking to enter into and argue to the jury that our clients caused the death of people. It doesn't get much more prejudicial than that and so we ask Your Honor when you look at this *Daubert*, when you consider the *Daubert* motions, to keep that framework in mind, that but for that count there would be no talk of death in this case. The connection that they are relying on to bring in this aspect of death into this case are these experts, so this is -- Part of the analysis is the prejudice. There is extreme potential prejudice in this case because of that dynamic.

THE COURT: If there is evidence introduced to that fact that he can't, especially if you file a motion in limine to prevent it.

MR. NIEWOEHNER: Understood. And, obviously, it will be under some *Daubert* motions and there are a number of things we will do to try to ensure that the evidence in this case is fairly brought.

THE COURT: I'm just saying. You are talking about testimony or opinion testimony that might be otherwise admissible. The prejudice that you are describing would be cured by that motion.

MR. NIEWOEHNER: I certainly appreciate -- We always appreciate the constructive criticism or advice.

THE COURT: No, I'm actual letter kind of asking.

MR. NIEWOEHNER: I think it would be part of what we will do down the road, but even in the *Daubert* context it still remains 403 as part of the analysis, so we are just emphasizing that there is the potential of significant prejudice here if experts come in and give opinions that they should not give because it should not survive scrutiny at the *Daubert*, we would hopefully not have to bring the motion in limine. But I'm just -- I appreciate your comments as well. Thank you, Your Honor.

So this case for us for Dr. Bonkovsky boils down to reliability. The foundation of his testimony is the medical records, either the patient records he himself has reviewed or the ones that form the basis for the articles and he agrees with our central premise that I've argued to you that if those medical records are inaccurate or interpreted inaccurately or misstated or incomplete, we're get garbage in and garbage out. His opinion is relevant -- The reliability of his opinion depends fully on whether that initial analysis was done correctly or not and we submit that Your Honor doesn't have a record to say that his opinion is reliable. And there is -- We've had conversation this morning about the appropriate evidence Your Honor would view and we submit that the cases in

our brief that we gave to you, the *Guillory* case, the *Christopherson* case, the *Vitago* case are good examples of what we think the correct path would be when we think about the reliability here which is you have to look at the underlying facts to assess the methodology.

We, as the record stands today, what we know from Dr. Bonkovsky is that there are some patient records he found that confirm his opinion and some that did not. There are some case studies in the articles that did and some that did not. What we don't know today is which is which and that's the critical inquiry from our perspective that if you are trying to determine whether he is reliable, you don't know on a given patient which way he went and if I don't know which way he went, you can't rely on it.

THE COURT: Sounds like a good jury argument.

MR. NIEWOEHNER: We will, Your Honor, put the Government to its burden. It is their burden to prove it. We submit they have not. We submit that we need this to understand this methodology and we think this gives you two choices, essentially, from our perspective. One would be to agree with me that this is inherently unreliable. A second would be to remedy the situation for us, because we truly cannot be in a situation, a trial without having two stacks of binders and having no clue which documents he thinks are or aren't relevant.

THE COURT: Although you weren't able to give it here is because of the nature of -- You will be able to ask him about each of those at trial, wouldn't you?

MR. NIEWOEHNER: But putting us in a situation at trial, live, having to cross him live, about 50 records for which I myself -- I dabble in hepatology at this point in my life but I'm not exactly a hepatologist myself. But point of Rule 16, the point of the *Daubert* procedure, the point of unfairness would require the Government to give us that information in advance, which they have, or could obtain, and so we ask Your Honor in the alternative, if you are unpersuaded by our efforts to suggest that the expert is unreliable in and of himself, to give us a lesser remedy, which would be to require the Government to give the information to which we need to assess which patient records he found reliable and which he did not, which case studies did he and which did he not, all easily within their power to give us that have the effect of preventing undue surprise, it would, quite frankly, be consistent with the requirements under Rule 16, and I think it would be appropriate in the circumstance of this case, simply given the prejudice that I just started with.

So I think those are the arguments from the USPLabs, Your Honor. Thank you.

THE COURT: And I'm assuming that the other Defense

counsel adopt those arguments unless they tell never otherwise? Mr. Gibson.

MR. GIBSON: Yes, ma'am. We adopt them, Your Honor.

THE COURT: Is there any other Defense counsel that wishes to present additional argument?

A bit of a housekeeping matter before we go on, too. I have these exhibits, these binders of exhibits. Are they offered for purposes of this hearing? Also, there was an MedWatch report that was marked. It was during Dr. Klontz's testimony. Is that being offered? I've only heard, that I can recall, one exhibit offered during the hearing although we were referred to many by both sides. Are they being offered?

MR. NIEWOEHNER: On behalf of USPLabs, Your Honor, yes.

MR. RUNKLE: Your Honor, we don't object to that, but as the Rules of Evidence don't apply at this type of a hearing, I don't know that they are actually being admitted into evidence. I think they are being --

THE COURT: Well, the problem is when there is an appeal, notice I said "when," when there is an appeal, on the record that gets sent to be reviewed by the district judge and should contain everything. If you have not offered them then they are not going to be part of that record that's reviewed. I'm just asking.

MR. LINEHAN: Your Honor, with respect to -- I'm sure

with respect to Dr. Bonkovsky and I'm sure with respect to Dr. Klontz, not all of the documents in the binder were actually used with the witness. It may make sense to go back and for us to sort of compile from both binders which ones were actually used and have those submitted and offered.

THE COURT: So are you going to offer them only those you used?

MR. LINEHAN: Correct.

THE COURT: Is there any objection to that?

MR. RUNKLE: No. There's not, Your Honor.

THE COURT: Then I'm going to admit those and you can cull those down to those exhibits then.

MR. RUNKLE: And if you could just put on the record that they're not being admitted into evidence for the case. Is that --

THE COURT: I said for the purposes of this hearing. I'm sorry.

MR. RUNKLE: Thank you, Your Honor.

MR. SULLIVAN: Your Honor, the only -- the only I guess exhibit the Government offered with Dr. Bonkovsky was his updated CV. That's what we offered up for the record. I think it was but I'm just making sure.

THE COURT: I think that was the only exhibit -- offered exhibit. Okay.

MR. RUNKLE: Your Honor, just a few very quick

points, Your Honor.

In terms of the evidence of benefit, I think Your Honor got it exactly right, that Dr. Bonkovsky's opinion is that there was no evidence of any benefit in any of the materials that he considered. I think he's entirely capable of offering that opinion as a physician, as a hepatologist. The -- Mr. --

THE COURT: Would you -- You think that's an opinion?

MR. RUNKLE: What did you say?

THE COURT: You think that's an opinion?

MR. RUNKLE: An opinion? No. That is -- That is his review of records about whether there's any evidence of benefit. I mean, that's a statement of fact about whether there's a benefit.

THE COURT: You said "opinion." I'm just trying to clarify.

MR. RUNKLE: I'm sorry, Your Honor. His opinion is about -- I think we all know what his opinion is and I think the evidence of benefit is a minor adjunct to his opinion. It's more of a factual statement of fact.

In terms of the prejudice Mr. Niewoehner is talking about, obviously, there are many other motions pending in this case. One of the motions we are not considering today is about severing count 10. I think that there's a lot of argument in that motion about why count 10, the injuries, the

liver injuries, are not just this creature of count 10. The liver injuries are relevant to the fraud count in part in count 1, and especially they are relevant to the obstruction count in count 6 because the liver injuries help, among other things, establish the state of mind of the defendants when they tried to ship this dangerous product away from where FDA was so that FDA couldn't find it, and so the knowledge of the liver injuries, any expert testimony about the liver injuries is very relevant to his other counts.

That's not what we are here to talk about today. We are also not here to talk about Rule 403 today. We are not doing motions in limine today. And so my only real response to that is that if the evidence is there and if they keep contesting the idea that people were actually injured by this product and people were injured by this product, there will being a factual basis at trial to put on people who were injured by it, families of people who died, and I understand that death is a large topic, but if it's contested whether this product caused injuries and Judge Lindsey finds that there's a reason to admit evidence about whether people died, that's just going to happen, and so I don't think that -- more relevant to today, I don't think that Dr. Bonkovsky is our way of getting evidence in the case that we would otherwise not enter into the case, if that's -- if that makes any sense.

Also, Mr. Niewoehner in his last point about the

reliability of these records, I think Your Honor already discussed how that sounds like a factual dispute for the jury and it sounds like a jury argument.

Mr. Niewoehner in other his other request that the Court ordered us to, I don't know, I guess generate a document about which patient record he found the most compelling and which ones he found the least compelling, I believe that we don't have any real obligation to do that. I think that we've already turned over the records. They have them. They can evaluate them with their experts who they -- they have plenty of experts who can do it also and it just becomes a factual dispute at trial.

I would also point out the Government, in its responses to the Defendants' experts, when you point it out where we believe the experts -- where we believe the expert disclosures were deficient, that was a year ago and we haven't heard one word about how they think Dr. Bonkovsky's expert disclosure under Rule 16 is deficient and I think that it's inappropriate to come here after a year to the *Daubert* hearing and then make a request that Rule 16 obligated us to turn something over that they could have raised that issue a year ago. That's my last point.

Thank you, Your Honor.

THE COURT: What about additional argument as to Dr. Klontz? Motion to exclude testimony or --

MR. LINEHAN: Thank you, Your Honor. I will be brief. Your Honor, you know -- you are, based on your briefing, you are aware of the *Daubert* standards and all the case law. With respect to the methodology that Dr. Klontz employed in this case and coming to his expert opinion, I think the case law is pretty strong on the idea that there needs to be a -- a descriptive and analytical component to an epidemiological study. We cite *Brock* for that proposition. We're not questioning -- I know there was some discussion about the timing and whether or not a control group could have been used. We're not necessarily questioning the wisdom of what happened in October 2013. I sure in Dr. Klontz's mind there was a need to move fast, but here we are two years later -- more than that -- five years later and we are still looking at what is only a descriptive epidemiology. There was plenty of time to do something more than that and it hasn't been done. Without it -- Without analytical epidemiology we have no mathematical measurement of what the likelihood of risk is.

On count 10 the Defendants in this case have been charged with distributing an adulterated product which is defined as a product that presents an unreasonable or a significant or unreasonable risk. We think that's a hopelessly vague standard, from a constitutional standard, and without expert testimony that actually puts mathematical

precision on the significance of the risk that was posed by this product. We think it's important that opinion be excluded.

In terms of what other things Dr. Klontz failed to do, he testified there was no -- he testified there was no rigid application of the Bradford Hill factors. There's case law to suggest without those factors an epidemiological opinion should be excluded under *Daubert*.

He said that -- And going back to the discussion, he does a descriptive epidemiology. He says it's only done in rare cases. Rare cases where the association is strong and I think we've established through his testimony that the methodology he took was far less than strong to establish an association that would warrant overlooking the absence of analytical epidemiology. He -- When we looked at his epidemiological curves, he did not -- he relied on unreliable MedWatch reports which he himself or others solicited from doctors with express reference to OEPNF. There was no consideration of the fact that -- In interpreting the spike in September, there was no consideration of the fact there was heavy media bias going on at the same time. There was no consideration of the fact that most of the tests on these patients were not done. In fact, close to half or over half of these tests that he said himself he set his own standard in terms of what was required in terms of excluding alternative

clauses and that standard was not met. I know, the -- the -- He did not dispute any of the numbers that I gave with respect to which -- how many patients were missing, how many were missing the various tests that he says were required.

And then, finally, he did no review to determine biological plausibility which is another factor under Bradford Hill. He cites a 1985 article. There were at least twelve articles that he could have found doing a comprehensive literature review. He doesn't that that. He was unaware of an FDA -- two FDA sponsored studies.

And I guess my final point, Your Honor, is that he's essentially reviewing his own work. This is not an objective expert who is stepping in and looking at the facts and says, you know what, there was a strong likelihood that OEP caused. This is someone that actually made the decision in a rush in October 2003 and now -- and --

THE COURT: 2013.

MR. LINEHAN: I'm sorry. 2013 and now five years later he is now examining his own work. Students don't it get to it grade their own work. It requires a more objective analysis and that's not here. He's essentially grading himself, so with that I believe that Dr. Klontz's testimony should be excluded under *Daubert*.

THE COURT: Okay. Any other Defense counsel want to chime in with something additional, so that the prosecutor has

an opportunity to respond that that.

MR. RUNKLE: Very briefly, Your Honor. First of all, I think the last argument about Dr. Klontz reviewing his own work is a classic sort of bias and credibility argument that goes to the weight of the evidence and not to admissibility. In addition, Dr. Klontz -- It reflects the obviously fact that Dr. Klontz is also a fact -- could be a fact witness in this case, but he also is an expert.

Now, in terms of the tests that Mr. Linehan talked about, I think Dr. Klontz was very clear that the tests were not required of every patient for his methodology to be effective, that it would be impossible to test or impractical or it simply wouldn't happen, he had to take the medical records as he found them. And so, for example, the fact that half of the patients may not have been tested for one virus and some other subset of patients may not have been tested for another virus has nothing to do with whether he could or couldn't identify the common element which was OxyElite Pro New Formula.

The other and more general fact, and this -- or more general legal argument, and this is part of the briefs that we've written but I want to apply it to what Mr. Linehan just said is that the case law the Defendants are talking about in terms of Dr. Klontz and epidemiology are essentially a reversal of the scenario that we are talking about in this

case. Those cases are about whether a epidemiological evidence of a general -- a general ability to cause a problem could be applied to a specific toxic tort or products liability plaintiff, and so it's essentially a fundamentally different concept than what we are doing in this case. We are not trying to nor do we need to prove proximate cause for any single patient and so courts are very skeptical about the idea that, okay, in some theoretical vacuum there's epidemiological evidence that some sort of substance could cause this illness that this plaintiff happens to have and courts are very skeptical about applying that -- that type of a test or that type of evidence without the type of analytical rigor that Mr. Linehan is talking about. This is a completely different case. This is not a toxic tort or a products liability case.

What we are proving here is not specific causation but rather risk and the risk is exactly what Dr. Klontz's opinion had a perfect fit for what we need to prove in this case. He is saying that there is an epidemiological association descriptively between this substance and dozens of liver injuries that can't be explained any other way. That's exactly part of what we need to prove on count 10. We do not need to prove in that any -- any specific illness was proximately caused by OxyElite Pro and that would be the type of evidence -- that would be the type of situation where you would want some sort of confidence in a rule, some sort of P

value as to where a specific illness was caused by that.

THE COURT: It wasn't clear to me how he came to the conclusion, that part of his conclusion, that the injuries could be caused no other way.

MR. RUNKLE: Well, his conclusion was that based on his experience as a epidemiologist and based on his review of this record that there was no other common element and also that the reports he talked about --

THE COURT: He didn't specifically review for commonality, which it sounded like he didn't. You heard that he did?

MR. RUNKLE: He did review for commonality. He said that he excluded -- from these records, he excluded other common causes. So, for example, when Mr. Linehan said 28 of, you know, something like 28 of the patients weren't tested for some virus but that means that the other 20 whatever were and that means that that can't be the common cause of the injuries. That's what he said.

THE COURT: Well, not one particular thing. They went through several different types of other conditions. But the point is that there could be some other factors that he didn't account for in determining based on the fact that these people have liver injury and these people also took this product and used this product and nothing else.

MR. RUNKLE: Well, I think that's essentially a fact

issue about each patient. I think that his --

THE COURT: Well, we have to get to the point that his opinion is sufficiently supported. You can't call everything a fact issue.

MR. RUNKLE: That's correct.

THE COURT: At some point his opinion has to meet certain requirements for him to be able to give it. We just don't let everybody give an opinion. There has to -- there has to be a reliable basis for it, so that's what I'm asking about.

MR. RUNKLE: And the reliable basis is the idea that when he reviewed these records there was no other common element that could explain this and then given his experience, your heard about his experience in studying outbreaks --

THE COURT: Oh, I heard about his experience in determining that in another situation that tomatoes caused the problem and then later he discovered that something else caused the problems which to me would make it important to know or to be able to exclude because both doctors said that this is a situation of exclusion. For him to -- for him to have some basis to exclude some other cause --

MR. RUNKLE: I think the distinction is between -- I'm sorry, Your Honor. I think the distinction is between hepatology and epidemiology. An epidemiologist is not a hepatologist and so there were questions about all these other

causes. He is looking at it from a epidemiological standpoint and deciding based on his experience in his 30 years --

THE COURT: But he said that's important.

MR. RUNKLE: He said it was important because it's a differential diagnosis. It's a diagnosis of exclusion. He said he didn't do that amongst the records that he reviewed. He said that on the record. He said that he reviewed them for other potential causes.

THE COURT: And what is the definition of an outbreak? Because I'm looking at one case here and one case there and several cases in Hawaii, really only several cases in Hawaii. What constitutes an outbreak so that we are talking about epidemiology?

MR. RUNKLE: So an outbreak I believe is a collection of unexplained diseases that seem -- that could be caused by a specific source. I think we talked --

THE COURT: What quantity is enough to be a collection to constitute an outbreak? Because it seems like a relatively small --

MR. RUNKLE: Yes.

THE COURT: -- to me. I'm asking --

MR. RUNKLE: I believe Dr. Klontz called this to me to be an epidemic to me, this type of an unexplained, very severe illness that -- an unexplained cluster of severe illnesses --

THE COURT: But the only place there is a cluster is Hawaii.

MR. RUNKLE: Well, there's a cluster because he said it's national in scope. I think he did talk about the national scope of an epidemic and that if it is contained in terms of geography, then maybe it's not an outbreak. But this had a national scope.

THE COURT: It seems to me that if you take the OEP out of mix then there's no reason to even consider it just based on the small number of cases, considering that something is happening.

MR. RUNKLE: I don't believe it a small -- 55 people or 70 people is not -- who have unexplained liver failure -- is not a small matter to the FDA. I can just tell you that.

THE COURT: I didn't say it's a small matter. I'm not even talking about a regulatory matter. I'm talking about the basis for finding his opinion for this criminal case.

MR. SULLIVAN: Your Honor, if I may.

THE COURT: Yes.

MR. SULLIVAN: You just said by taking OxyElite Pro out of the mix. That's what happened. There was a recall. OxyElite Pro was taken out of the public consumption in November. As through Mr. Linehan's questioning, the injury reports as to OxyElite Pro almost disappear; the last one appearing in February of 2014. So you are right. If you take

it out of the mix we should have something happen and something did happen.

MR. RUNKLE: That's all we've got, Your Honor. Thank you.

THE COURT: You look like you want to say something.

MR. LINEHAN: Kind of. May I?

THE COURT: Brief. This is your motion.

MR. LINEHAN: Right. I know that the word "outbreak" has been used and I know you asked about the definition. Dr. Klontz offered no definition for outbreak. I'm not sure what he means by "outbreak." What we have is we have 55 patients, not 70, at least not based on the disclosure because the disclosure talks about 55. His article talks about 55, so it's based on 55, most of which are in Hawaii, some of which are sort of scattered here and there, based on MedWatch reports that he asked for, okay.

MS. MARTIN: Your Honor, let me just object quickly. Mr. Linehan keeps -- keeps misrepresenting to the Court the disclosures only mention 55. Only mention 55. That's not accurate. The MedWatch reports 55. Also on page 55 of this document he talks --

THE COURT: Of the disclosure?

MS. MARTIN: Of the disclosure. He talks about patient medical records and from MedWatch reports. That's just a misrepresentation that he continues to make and I

wanted to point it out to the Court.

MR. LINEHAN: The article and the disclosure talk about 55 patients whose liver injury is likely caused by OEPNF. I don't see any other discussion about any more than that.

And I guess the only other point I would address Mr. Sullivan's point which is once they lifted -- once they lifted the product from the market it stopped -- that the adverse events stopped. These were adverse events that they were collecting themselves. These are not natural adverse events. And we had -- And Dr. Klontz, who said himself that he didn't check -- There's no evidence -- He didn't look at any -- any data or evidence that there were reports of liver injury after, you know, after late 2013 or early 2014, so with that we are finished, Your Honor.

THE COURT: Okay. As to the Defense motion to exclude Dr. Bonkovsky's testimony, I'm going to deny it and I will issue a written opinion that explains in more detail why.

As to the Defense motion, I think it's No. 278, is the one that -- to exclude Dr. Klontz's opinion testimony, and this is only to the opinion testimony, because I agree with prosecutors that he may be appropriately a fact witness, but as to the opinion that I've been told he is about to give today, I don't find that it meets the reliability standard set forth in *Daubert* in Rule 702 and so I'm going to grant the

Motion to Exclude that and I will issue a written opinion that explains that in more detail.

Okay. As far as the other motions to exclude, let's do the Defense ones first. Is there additional evidence that's going to being discussed? I understand there is no testimony or evidence that you are going to introduce today on those?

MR. LINEHAN: Your Honor, I think -- The way we wrote these down, correct me if I'm wrong, I'm not sure if any of the others Motions to Exclude were on the agenda today.

THE COURT: We actually had a whole laundry list to give you an opportunity -- Where is notice and I will have a look. We informed you that we were going to hear motions 220, 221. Those are two motions to dismiss. 251, that's a Motion to Exclude the Testimony of Catherine Tucker. 252, the Motion to Exclude the Testimony of Nicholas Oberlies. 253, Motion to Exclude Expert Testimony of Drs. Gurley, Koturbash, and Boerma. And documents 256, motion to exclude the testimony of Dr. Mahmoud Elsohly.

MR. LINEHAN: Your Honor, if you can --

MR. GIBSON: Can we have a chance before the Court --

THE COURT: Sure.

MR. GIBSON: I'll be honest with you, we're not seeing that on an order as to what we were going to address and I suspect both sides are not prepared to address them.

But I don't know how best to work it out with the Court, but --

MR. MCMULLEN: If I may, Your Honor, we -- Your Honor, Jeff McMullen, if I may. The hearing orders that we reviewed were document 439 and document 435.

THE COURT: Yes.

MR. MCMULLEN: And those were the only two we reviewed.

THE COURT: Those should be the only two, but I could have sworn that I told you --

(Off-the-record with law clerk.)

THE COURT: So they should have been -- You should be able to read them if you are not able to -- For some reason I'm having trouble here. That's why I started this hearing by saying we would go with the ones we have first when I realized we only had two witnesses.

MR. GIBSON: Judge, I think also, if you will look at document 343, that's Judge Lindsay's order of reference and those were referred to the Court but, again, as Mr. McMullen said, we are relying on document 435 and 439 where you tell us to be prepared to call witnesses and argue on certain motions. Those motions are not -- or at least what I -- what we have, Judge, and, again, I -- I can assure you we would have been prepared if we had all understood it, without question.

MR. MCMULLEN: I have docket 435 on my iPad, which is

the Court's order, and then 439 I believe was just a minute order put on the docket. It doesn't have an associated document without listing the additional items.

(Off-the-record discussion between Court and law clerk.)

THE COURT: It looks like they are all listed. Several are listed in 435. Every one I've named so far. I guess I'm -- I guess I'm missing the point. Let me have that document, please.

MR. GIBSON: Can we go check the number, Your Honor? We want to be accurate and be prepared.

THE COURT: Sure.

MR. GIBSON: This is document 435 filed on April the 10th, and it's -- and it's -- it's your order.

THE COURT: Yes.

MR. GIBSON: It is ordering us in the first part, the following motions: Document 220, Motion to Dismiss Count 10, which we're prepared to argue. Motion to -- Docket 220, Motion to Dismiss Counts 9 and 10 For Unconstitutional Vagueness. We are prepared to address 221. That's Dr. Bonkovsky 's -- Bonkovsky's testimony.

THE COURT: Yes.

MR. GIBSON: 277 is Dr. Klontz's testimony. Then the next one -- The next one on that order is 293 which is my Motion to Dismiss Count 10, 392. And then you tell us that those documents that -- as to these motions documents 220,

277, and 278 will convene a *Daubert* hearing just on those documents. I think that's how we interpreted it. Let me say that.

MR. RUNKLE: Your Honor, did you determine that a *Daubert* hearing wasn't necessary on the other motions to exclude?

THE COURT: I actually formed an opinion as to them but I was offering the opportunity I believe to -- to offer something on the record.

MR. RUNKLE: We'd like to hear your opinion, Your Honor.

MR. GIBSON: If you want to give us a cursory review.

THE COURT: If I did not do that, then -- You tell me which ones you want to offer some testimony on and we'll just reconvene later on those.

MR. GIBSON: Can we do that?

THE COURT: Yes, we can. Which ones can you -- that you -- which ones -- motions to exclude you were not prepared to go on that you want to offer some testimony?

MR. GIBSON: We're going to have to -- Can we collectively -- I can give you my opinion, but not for everybody. I mean, can we -- Do you want us to take a break and do that? Is that what you are suggesting?

THE COURT: Sure. So I know which way we are going.

MR. GIBSON: Okay.

MR. RUNKLE: Your Honor, I don't -- I don't believe 245 -- I guess -- their motion to exclude our witnesses --

THE COURT: There doesn't always have to be a -- I mean, you can -- you can have a -- you can make a decision on the submissions of the exhibits that were presented which I am prepared to do. But if you -- I did have specific questions, as you probably noticed, about Dr. Bonkovsky -- both Dr. Bonkovsky and Dr. Klontz, and that's probably why it was more specific. But, yes, it was my intention though that we consider all those that had been referred, so if I didn't make that clear, then I'm willing to reconvene if you want to present something more than what you've already presented on the other motions to exclude.

MR. RUNKLE: Your Honor, given the situation, I don't believe the Government would need to put those witnesses on. I mean, if -- if Your Honor's determination is you can decide it on the papers, it's a motion to exclude our witnesses --

THE COURT: I believe that I can but I'm -- I don't want to -- since we are having a hearing anyway, I -- Like I said, if there's a misunderstanding you would like to present --

MR. GIBSON: Your Honor, if I may ask and the suggestion may be then with regard to your timetable then, if we can -- we have these other motions, substantive motions that I think we are prepared to go forward on.

THE COURT: The motions to dismiss?

MR. GIBSON: The motions to dismiss.

THE COURT: Okay.

THE CLERK: And then if possible -- and that has us the evening to look at it --

THE COURT: I will ask you to give me a status report, a joint one, regarding whether or not you want a live hearing on documents 251, motion to exclude Tucker. Document 252, motion to exclude Oberlies. Document 253, motion to exclude Drs. Gurley, Koturbash, and Boerma. Document 256, motion to exclude Dr. Elsohly. And also the motions filed by the Government regarding -- including 259, 260, 261, 262, 263, 264, 265, 266, 267. So 259 through --

MR. GIBSON: 267?

THE COURT: -- 267 as well.

MR. GIBSON: Yes, ma'am. I will give you that report either late tonight or in the morning.

THE COURT: Yes. Tomorrow is fine.

MR. GIBSON: Thank you, Your Honor. I apologize for the confusion.

THE COURT: No. It's my fault. I do, too. So can we go ahead and hear -- I'm assuming you are just offering additional arguments on the motions to dismiss?

MR. LINEHAN: Yes, Your Honor.

THE COURT: Okay. Who want to proceed?

MR. LINEHAN: Does the Court have a preference for which one you want to hear first?

THE COURT: I would just like to two through them. Several of them seem to relate to each other and they relate to the same counts, so --

(Recess.)

I, **DENVER B. RODEN**, United States Court Reporter for the United States District Court in and for the Northern District of Texas, Fort Worth Division, hereby certify that the above and foregoing contains a true and correct transcription of the proceedings in the above entitled and numbered cause.

WITNESS MY HAND on this 12th day of June, 2018.

/s/ Denver B. Roden

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